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(54) Title: **PROTEIN KINASES**

(57) Abstract: The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

DESCRIPTION  
PROTEIN KINASES

FIELD OF THE INVENTION

5           The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

BACKGROUND OF THE INVENTION

10           The following description of the background of the invention is provided to aid in understanding the invention, but is not admitted to be or to describe prior art to the invention.

          Cellular signal transduction is a fundamental mechanism whereby external stimuli that regulate diverse cellular processes are relayed to the interior of cells. One of the key  
15           biochemical mechanisms of signal transduction involves the reversible phosphorylation of proteins, which enables regulation of the activity of mature proteins by altering their structure and function.

          Protein phosphorylation plays a pivotal role in biological signal transduction. Among the biological functions controlled by protein phosphorylation are the following:  
20           cell division; differentiation and death (apoptosis); cell motility and cytoskeletal structure; control of DNA replication, transcription, splicing and translation; protein translocation events from the endoplasmic reticulum and Golgi apparatus to the membrane and extracellular space; protein nuclear import and export; regulation of metabolic reactions, etc. Abnormal protein phosphorylation is widely recognized to be causally linked to the  
25           etiology of many diseases including cancer as well as immunologic, neuronal and metabolic disorders.

          The most common phospho-acceptor amino acid residues are serine, threonine and tyrosine. Phosphorylation in histidine has also been observed in bacteria. The presence of a phosphate moiety modulates protein function in multiple ways. A common mechanism  
30           includes changes in the catalytic properties ( $V_{max}$  and  $K_m$ ) of an enzyme leading to its activation or inactivation. A second widely recognized mechanism involves promoting protein-protein interactions. An example of this is the tyrosine autophosphorylation of the



ligand-activated EGF receptor tyrosine kinase. This event triggers the high-affinity binding to the phosphotyrosine residue on the receptor's C-terminal intracellular domain to the SH2 motif of the adaptor molecule Grb2. Grb2 in turn binds through its SH3 motif to a second adaptor molecule, such as SHC. The formation of this ternary complex activates the signaling events that are responsible for the biological effects of EGF. Serine and threonine phosphorylation events have also been recently recognized to exert their biological function through protein-protein interaction events mediated by the high-affinity binding of phosphoserine and phosphothreonine to WW motifs present in a large variety of proteins (Lu, P.J. *et al.* (1999) *Science* 283:1325-1328). A third important outcome of protein phosphorylation is changes in the subcellular localization of the substrate. As an example, nuclear import and export events in a large diversity of proteins are regulated by protein phosphorylation (Drier E.A. *et al.* (1999) *Genes Dev* 13: 556-568).

Protein kinases are one of the largest families of eukaryotic proteins with several hundred known members. These proteins share a 250-300 amino acid domain that can be subdivided into 12 distinct subdomains that comprise the common catalytic core structure. These conserved protein motifs have recently been exploited using PCR-based and bioinformatic strategies leading to a significant expansion of the known kinases. Multiple alignment of the sequences in the catalytic domain of protein kinases and subsequent parsimony analysis permits their segregation into a dendrogram reflecting the relatedness of their catalytic domains (Fig. 1). In this manner, related kinases are clustered into distinct branches or subfamilies including: tyrosine kinases, cyclic-nucleotide-dependent kinases, calcium/calmodulin kinases, cyclin-dependent kinases and MAP-kinases, serine-threonine kinase receptors, and several other less defined subfamilies.

We have recently completed a systematic analysis of the protein kinases present in *C. elegans*, the multicellular organism whose entire DNA sequence has been determined. We identified 473 unique kinase profiles including 398 full-length conventional kinases, and 20 additional proteins that may function as atypical protein kinases. (Plowman G.D. *et al.* (1999), *Proc. Natl. Acad. Sci.* 96:13603-13610).

Using parsimony analysis, the protein kinases may be divided into 4 major groups: AGC, CAMK, CMGC and tyrosine kinases. In addition, there are a number of minor yet distinct families, including the STE and casein kinase 1, families related to worm- or

fungus-specific kinases, and a family designated "other" to represent several smaller families. In addition, we designate an "atypical" family to represent protein kinases whose catalytic domain has little or no primary sequence homology to conventional kinases, including the A6 kinases and PI3 kinases.

5       The AGC kinases are basic amino acid-directed enzymes that phosphorylate residues found proximal to Arg and Lys. Examples of this group are the cyclic nucleotide-dependent kinases, G protein kinases, NDR or DBF2 and the ribosomal S6 kinases.

      The CAMK group kinases are also basic amino acid-directed kinases. They include the Ca<sup>2+</sup>/calmodulin-regulated and AMP-dependent protein kinases, myosin light chain  
10       kinases, checkpoint 2 kinases (CHK2) and EMK-related protein kinases. The EMK family of STK are involved in the control of cell polarity, microtubule stability and cancer. One member of the EMK family, C-TAK1 has been reported to control entry into mitosis by activating Cdc25C which in turn dephosphorylates Cdc2.

      CMGC group kinases are "proline-directed" enzymes phosphorylating residues  
15       that exist in a proline-rich context. They include the cyclin-dependent kinases (CDKs), mitogen-activated kinases (MAPKs), GSK3s and CLKs. Most CMGC kinases have larger-than-average kinase domains owing to the presence of insertions within subdomains X and XI.

      The tyrosine kinase group encompass both cytoplasmic (i.e. src) as well as  
20       transmembrane receptor tyrosine kinases (i.e. EGF receptor). These kinases play a pivotal role in the signal transduction processes that mediate cell proliferation, differentiation and apoptosis.

      Group members that define smaller, yet distinct phylogenetic branches of  
25       conventional kinases include the elongation factor 2 kinases (EFKs); homologues of the yeast sterile family kinases (STE) which refers to 3 classes of kinases which lie sequentially upstream of the MAPKs; mixed lineage kinases (MLKs); Lim-domain containing kinases (LIMKs); Calcium-calmodulin kinase kinases (CAMKK), dual-specific tyrosine kinases (DYRK), integrin receptor associated kinase (IRAK); testis-specific  
30       kinases (TSK); UNC-51 related kinases (UNC); several families that are close homologues to worm (C26C2.1, YQ09, ZC581.9, YFL033c, C24A1.3), *Drosophila* (SLOB), or yeast (YDOD\_sp, YGR262\_sc) kinases, and others that are "unique" and don't cluster into any obvious family.

## SUMMARY OF THE INVENTION

Through a search of the EST database for homologies to the conserved catalytic kinase domain of protein kinases, hundreds of mammalian members of known and previously unidentified protein kinase families and groups have been identified as part of the present invention. Multiple alignment and parsimony analysis of the catalytic domain reveals that approximately half of these protein kinases cluster into 10 known groups, with the other half perhaps defining novel groups. Classification in this manner has proven highly accurate not only in predicting motifs present in the remaining non-catalytic portion of each protein, but also in their regulation, substrates, and signaling pathways. The present invention includes the partial or complete sequence of new protein kinases, their classification, predicted or deduced protein structure, and a strategy for elucidating their biologic and therapeutic relevance.

Thus, a first aspect of the invention features an isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211.

SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
5 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
and SEQ ID NO:242.

By "isolated" in reference to nucleic acid is meant a polymer of nucleotides  
conjugated to each other, including DNA and RNA, that is isolated from a natural source  
10 or that is synthesized. The isolated nucleic acid of the present invention is unique in the  
sense that it is not found in a pure or separated state in nature. Use of the term "isolated"  
indicates that a naturally occurring sequence has been removed from its normal cellular  
(i.e., chromosomal) environment. Thus, the sequence may be in a cell-free solution or  
placed in a different cellular environment. The term does not imply that the sequence is  
15 the only nucleotide chain present, but that it is essentially free (about 90 - 95% pure at  
least) of non-nucleotide material naturally associated with it, and thus is distinguished  
from isolated chromosomes.

By the use of the term "enriched" in reference to nucleic acid is meant that the  
specific DNA or RNA sequence constitutes a significantly higher fraction (2 - 5 fold) of  
20 the total DNA or RNA present in the cells or solution of interest than in normal or  
diseased cells or in the cells from which the sequence was taken. This could be caused by  
a person by preferential reduction in the amount of other DNA or RNA present, or by a  
preferential increase in the amount of the specific DNA or RNA sequence, or by a  
combination of the two. However, it should be noted that enriched does not imply that  
25 there are no other DNA or RNA sequences present, just that the relative amount of the  
sequence of interest has been significantly increased. The term "significant" is used to  
indicate that the level of increase is useful to the person making such an increase, and  
generally means an increase relative to other nucleic acids of about at least 2 fold, more  
preferably at least 5 to 10 fold or even more. The term also does not imply that there is no  
30 DNA or RNA from other sources. The other source DNA may, for example, comprise  
DNA from a yeast or bacterial genome, or a cloning vector such as pUC19. This term  
distinguishes from naturally occurring events, such as viral infection, or tumor type

growths, in which the level of one mRNA may be naturally increased relative to other species of mRNA. That is, the term is meant to cover only those situations in which a person has intervened to elevate the proportion of the desired nucleic acid.

It is also advantageous for some purposes that a nucleotide sequence be in purified form. The term "purified" in reference to nucleic acid does not require absolute purity (such as a homogeneous preparation). Instead, it represents an indication that the sequence is relatively more pure than in the natural environment (compared to the natural level this level should be at least 2-5 fold greater, *e.g.*, in terms of mg/mL). Individual clones isolated from a cDNA library may be purified to electrophoretic homogeneity. The claimed DNA molecules obtained from these clones could be obtained directly from total DNA or from total RNA. The cDNA clones are not naturally occurring, but rather are preferably obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The construction of a cDNA library from mRNA involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection of the cells carrying the cDNA library. Thus, the process which includes the construction of a cDNA library from mRNA and isolation of distinct cDNA clones yields an approximately  $10^6$ -fold purification of the native message. Thus, purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

By a "kinase polypeptide" is meant 10 (preferably 20, more preferably 40, most preferably 75) or more contiguous amino acids set forth in an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,

SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
5 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,  
SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
10 SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional  
15 derivatives thereof as described herein. For sequences for which the full-length sequence  
is not given, the remaining sequences can be determined using methods well-known to  
those in the art and are intended to be included in the invention. In certain aspects,  
polypeptides of 100, 200, 300 or more amino acids are preferred. The kinase polypeptide  
can be encoded by a full-length nucleic acid sequence or any portion of the full-length  
20 nucleic acid sequence, so long as a functional activity of the polypeptide is retained. By  
"functional" domain is meant any region of the polypeptide that may play a regulatory or  
catalytic role as predicted from amino acid sequence homology to other proteins or by the  
presence of amino acid sequences that may give rise to specific structural conformations  
(*i.e.*, coiled-coils). For some purposes, polypeptide domains are preferred, including, but  
25 not limited to, N-terminal, catalytic/kinase and C-terminal.

The amino acid sequence will be substantially similar to a sequence selected from  
the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID  
NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID  
30 NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID  
NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID

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5 NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID  
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NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID  
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NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID  
NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding  
20 full-length amino acid sequence, or fragments thereof. A sequence that is substantially  
similar to a sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
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ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 or portions of or the entire corresponding full-length amino acid sequences.

By "identity" is meant a property of sequences that measures their similarity or relationship. Identity is measured by dividing the number of identical residues between two sequences (either full-length or a defined domain) by the total number of residues in the known sequence, or the domain of the known sequence, and multiplying the product by 100. Thus, two copies of exactly the same sequence have 100% identity, but sequences that are less highly conserved, and have replacements and substitutions, have a lower degree of identity. "Gaps" are spaces in an alignment that can result from aligning a novel sequence with a known sequence when the novel sequence has additions or deletions of amino acids in comparison with the known sequence. These gaps do not factor into the assessment of % identity using the above calculation.

Those skilled in the art will recognize that several computer programs are also available for determining sequence identity using standard parameters, for example, Blast (Altschul, *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402), Blast2 (Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-410), and Smith-Waterman (Smith, *et al.* (1981) *J. Mol. Biol.* 147:195-197).

In preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding a kinase polypeptide comprising a nucleotide sequence that: (a) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID

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NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID  
5 NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID  
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10 NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID  
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NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID  
NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will  
15 have at least 75% identity (preferably 90%, more preferably at least 95% and most  
preferably 99-100%) to the sequence selected from the group consisting of those set forth  
in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID  
NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID  
NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID  
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NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID  
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5 NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c)  
10 hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes  
a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an  
amino acid sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
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NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID  
NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID  
30 NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID  
NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID  
NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID

NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof.

A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID

NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
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5 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
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NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
25 ID NO:242, except that it lacks one or more, but not all, of a domain selected from the  
group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a  
coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-  
terminal tail; (e) is the complement of the nucleotide sequence of (d); (f) encodes a  
polypeptide having an amino acid sequence selected from the group consisting of those set  
30 forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID  
NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID  
NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID

NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID  
NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID  
NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID  
NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID  
5 NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID  
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NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
20 NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or  
fragments thereof. (The domain demarcations of the polypeptides of the invention are  
indicated in Table 2 by reference to the kinase domain.) A sequence that is substantially  
25 similar to a sequence selected from the group consisting of those set forth in SEQ ID  
NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
30 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID

NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ



ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID

NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof.

A sequence that is substantially similar to a sequence selected from the group consisting of

those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235,

SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to a domain of a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, where the domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (g) is the complement of the nucleotide sequence of (f); (h) encodes a polypeptide having an amino acid sequence selected from the group consisting

of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,

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5 SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
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10 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
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SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
15 SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
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SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
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25 NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
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NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID  
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NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID

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5 NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID  
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NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID  
10 NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
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30 NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID  
NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID

NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID  
NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID  
NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID  
NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID  
5 NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID  
NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID  
NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID  
NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID  
NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the  
10 corresponding full-length amino acid sequence, or fragments thereof. A sequence that is  
substantially similar to a sequence selected from the group consisting of those set forth in  
SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126,  
SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131,  
SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,  
15 SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146,  
SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151,  
SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156,  
SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
20 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,  
SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
25 SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
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SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
30 SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226.

SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more of the domains selected from the group consisting of a N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; or (i) is the



complement of the nucleotide sequence of (h). The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.

The term "complement" refers to two nucleotides that can form multiple favorable interactions with one another. For example, adenine is complementary to thymine as they can form two hydrogen bonds. Similarly, guanine and cytosine are complementary since they can form three hydrogen bonds. A nucleotide sequence is the complement of another nucleotide sequence if all of the nucleotides of the first sequence are complementary to all of the nucleotides of the second sequence.

The term "domain" refers to a region of a polypeptide that contains a particular function. For instance, N-terminal or C-terminal domains of signal transduction proteins can serve functions including, but not limited to, binding molecules that localize the signal transduction molecule to different regions of the cell or binding other signaling molecules directly responsible for propagating a particular cellular signal. Some domains can be expressed separately from the rest of the protein and function by themselves, while others must remain part of the intact protein to retain function. The latter are termed functional regions of proteins and also relate to domains.

The term "N-terminal domain" refers to the extracatalytic region located between the initiator methionine and the catalytic domain of the protein kinase. The N-terminal domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the N-terminal boundary of the catalytic domain. Depending on its length, the N-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose N-terminal domain has been shown to play a regulatory role is PAK65, which contains a CRIB motif used for Cdc42 and rac binding (Burbelo, P.D. *et al.* (1995) J. Biol. Chem. 270, 29071-29074). The N-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the amino-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. Further, in some cases, portions of the N-terminal domains of the protein kinases of the invention have not been identified since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined and using the approaches described herein the N-terminal domain can be identified.

The term "catalytic domain" or "kinase domain" refers to a region of the protein kinase that is typically 25-300 amino acids long and is responsible for carrying out the phosphate transfer reaction from a high-energy phosphate donor molecule such as ATP or GTP to itself (autophosphorylation) or to other proteins (exogenous phosphorylation).

5 The catalytic domain of protein kinases is made up of 12 subdomains that contain highly conserved amino acid residues, and are responsible for proper polypeptide folding and for catalysis. The catalytic domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database. The catalytic/kinase domains of the protein kinases of the invention are identified in Table 2, herein. Further,  
10 in some cases, the complete sequence of the catalytic/kinase domains of the protein kinases of the invention may not have been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the catalytic/kinase domain can be identified.

15 The term "catalytic activity", as used herein, defines the rate at which a kinase catalytic domain phosphorylates a substrate. Catalytic activity can be measured, for example, by determining the amount of a substrate converted to a phosphorylated product as a function of time. Catalytic activity can be measured by methods of the invention by  
20 holding time constant and determining the concentration of a phosphorylated substrate after a fixed period of time. Phosphorylation of a substrate occurs at the active-site of a protein kinase. The active-site is normally a cavity in which the substrate binds to the protein kinase and is phosphorylated.

The term "substrate" as used herein refers to a molecule phosphorylated by a kinase of the invention. Kinases phosphorylate substrates on serine/threonine or tyrosine  
25 amino acids. The molecule may be another protein or a polypeptide.

The term "C-terminal domain" refers to the region located between the catalytic domain and the carboxy-terminal amino acid residue of the protein kinase. The C-terminal domain can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the C-terminal boundary of  
30 the catalytic domain or of any functional C-terminal extracatalytic domain. Depending on its length and amino acid composition, the C-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose C-terminal

domain may play a regulatory role is PAK3 which contains a heterotrimeric  $G_b$  subunit-binding site near its C-terminus (Leeuw, T. *et al.* (1998) *Nature*, 391, 191-195). The C-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the carboxy-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. In some cases, the C-terminal domains of the protein kinases of the invention have not been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the C-terminal domain can be identified.

The term "signal transduction pathway" refers to the molecules that propagate an extracellular signal through the cell membrane to become an intracellular signal. This signal can then stimulate a cellular response. The polypeptide molecules involved in signal transduction processes are typically receptor and non-receptor protein tyrosine kinases, receptor and non-receptor protein phosphatases, SRC homology 2 and 3 domains, phosphotyrosine binding proteins (SRC homology 2 (SH2) and phosphotyrosine binding (PTB and PH) domain containing proteins), proline-rich binding proteins (SH3 domain containing proteins), nucleotide exchange factors, and transcription factors.

The term "coiled-coil structure region" as used herein, refers to a polypeptide sequence that has a high probability of adopting a coiled-coil structure as predicted by computer algorithms such as COILS (Lupas, A. (1996) *Meth. Enzymology* 266:513-525). Coiled-coils are formed by two or three amphipathic  $\alpha$ -helices in parallel. Coiled-coils can bind to coiled-coil domains of other polypeptides resulting in homo- or heterodimers (Lupas, A. (1991) *Science* 252:1162-1164). Coiled-coil-dependent oligomerization has been shown to be necessary for protein function including catalytic activity of serine/threonine kinases (Roe, J. *et al.* (1997) *J. Biol. Chem.* 272:5838-5845). Coiled-coil regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "proline-rich region" as used herein, refers to a region of a protein kinase whose proline content over a given amino acid length is higher than the average content of this amino acid found in proteins (*i.e.*, >10%). Proline-rich regions are easily discernable by visual inspection of amino acid sequences and quantitated by standard computer

sequence analysis programs such as the DNASTar program EditSeq. Proline-rich regions have been demonstrated to participate in regulatory protein -protein interactions. Among these interactions, those that are most relevant to this invention involve the "PxxP" proline rich motif found in certain protein kinases (*i.e.*, human PAK1) and the SH3 domain of the adaptor molecule Nck (Galisteo, M.L. *et al.* (1996) J. Biol. Chem. 271:20997-21000).

Other regulatory interactions involving "PxxP" proline-rich motifs include the WW domain (Sudol, M. (1996) Prog. Biophys. Mol. Bio. 65:113-132). Proline rich regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "spacer region" as used herein, refers to a region of the protein kinase located between predicted functional domains. The spacer region has no detectable homology to any amino acid sequence in the database, and can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the C- and N-terminal boundaries of the flanking functional domains. Spacer regions may or may not play a fundamental role in protein kinase function. Precedence for the regulatory role of spacer regions in kinase function is provided by the role of the src kinase spacer in inter-domain interactions (Xu, W. *et al.* (1997) Nature 385:595-602). Spacer regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "insert" as used herein refers to a portion of a protein kinase that is absent from a close homolog. Inserts may or may not be the product alternative splicing of exons. Inserts can be identified by using a Smith-Waterman sequence alignment of the protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNASTar program Megalign. Inserts may play a functional role by presenting a new interface for protein-protein interactions, or by interfering with such interactions. Insert regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "C-terminal tail" as used herein, refers to a C-terminal domain of a protein kinase, that by homology extends or protrudes past the C-terminal amino acid of its closest homolog. C-terminal tails can be identified by using a Smith-Waterman sequence alignment of the protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNASTar program Megalign. Depending on its length, a C-terminal tail may or may not play a regulatory role in kinase function. C-terminal tail regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

Various low or high stringency hybridization conditions may be used depending upon the specificity and selectivity desired. These conditions are well-known to those skilled in the art. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20 contiguous nucleotides, more preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 50 contiguous nucleotides, most preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 100 contiguous nucleotides. In some instances, the conditions may prevent hybridization of nucleic acids having more than 5 mismatches in the full-length sequence.

By stringent hybridization assay conditions is meant hybridization assay conditions at least as stringent as the following: hybridization in 50% formamide, 5X SSC, 50 mM  $\text{NaH}_2\text{PO}_4$ , pH 6.8, 0.5% SDS, 0.1 mg/mL sonicated salmon sperm DNA, and 5X Denhart solution at 42 °C overnight; washing with 2X SSC, 0.1% SDS at 45 °C; and washing with 0.2X SSC, 0.1% SDS at 45 °C. Under some of the most stringent hybridization assay conditions, the second wash can be done with 0.1X SSC at a temperature up to 70 °C (pg. 421, Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein including any figures, tables, or drawings.). However, other applications may require the use of conditions falling between these sets of conditions. Methods of determining the conditions required to achieve desired hybridizations are well-known to those with ordinary skill in the art, and are based on several factors, including but not limited to, the sequences to be hybridized and the samples to be tested.

In other preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding kinase polypeptides, further comprising a vector or promoter effective to initiate transcription in a host cell. The invention also features recombinant nucleic acid, preferably in a cell or an organism. The recombinant nucleic acid may contain a sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a functional derivative thereof and a vector or a promoter effective to initiate transcription in a host cell. The recombinant nucleic acid can alternatively contain a transcriptional initiation region functional in a cell, a sequence complementary to an RNA sequence encoding a kinase polypeptide and a transcriptional termination region functional in a cell. Specific

vectors and host cell combinations are discussed herein. The recombinant nucleic acid can also contain the full-length sequence encoding the protein kinase, or a domain, for example.

The term "vector" relates to a single or double-stranded circular nucleic acid molecule that can be transfected into cells and replicated within or independently of a cell genome. A circular double-stranded nucleic acid molecule can be cut and thereby linearized upon treatment with restriction enzymes. An assortment of nucleic acid vectors, restriction enzymes, and the knowledge of the nucleotide sequences cut by restriction enzymes are readily available to those skilled in the art. A nucleic acid molecule encoding a kinase can be inserted into a vector by cutting the vector with restriction enzymes and ligating the two pieces together.

The term "transfecting" defines a number of methods to insert a nucleic acid vector or other nucleic acid molecules into a cellular organism. These methods involve a variety of techniques, such as treating the cells with high concentrations of salt, an electric field, detergent, or DMSO to render the outer membrane or wall of the cells permeable to nucleic acid molecules of interest or use of various viral transduction strategies.

The term "promoter" as used herein, refers to nucleic acid sequence needed for gene sequence expression. Promoter regions vary from organism to organism, but are well known to persons skilled in the art for different organisms. For example, in prokaryotes, the promoter region contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

In preferred embodiments, the isolated nucleic acid comprises, consists essentially of, or consists of a nucleic acid sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35.

SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, encodes an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID



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NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
10 NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242, or the corresponding full-length amino acid sequence, a functional derivative  
thereof, or at least 10, 20, 40, 50, 75, 100, 200, 300 or 500 contiguous amino acids of a  
sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID  
15 NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID  
NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID  
NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID  
NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID  
NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID  
20 NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID  
NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID  
NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID  
NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID  
NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID  
25 NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID  
NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID  
NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID  
NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID  
30 NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID  
NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID  
NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID

NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length sequences or derivatives thereof. The nucleic acid may be isolated from a natural source by cDNA cloning or by subtractive hybridization. The natural source may be mammalian, preferably human, blood, semen, or tissue, and the nucleic acid may be synthesized by the triester method or by using an automated DNA synthesizer.

The term "mammal" refers preferably to such organisms as mice, rats, rabbits, guinea pigs, sheep, and goats, more preferably to cats, dogs, monkeys, and apes, and most preferably to humans.

In yet other preferred embodiments, the nucleic acid is a conserved or unique region, for example those useful for: the design of hybridization probes to facilitate identification and cloning of additional polypeptides, the design of PCR probes to facilitate cloning of additional polypeptides, obtaining antibodies to polypeptide regions, and designing antisense oligonucleotides.

By "conserved nucleic acid regions", are meant regions present on two or more nucleic acids encoding a kinase polypeptide, to which a particular nucleic acid sequence can hybridize under lower stringency conditions. Examples of lower stringency conditions suitable for screening for nucleic acid encoding kinase polypeptides are provided in Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables. Preferably, conserved regions differ by no more than 5 out of 20 nucleotides, even more preferably 2 out of 20 nucleotides or most preferably 1 out of 20 nucleotides.

By "unique nucleic acid region" is meant a sequence present in a nucleic acid coding for a kinase polypeptide that is not present in a sequence coding for any other naturally occurring polypeptide. Such regions preferably encode 10 (preferably 25, more preferably 50, most preferably 75) or more contiguous amino acids selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,

SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
5 SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
10 SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194,  
15 SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
20 SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional derivatives thereof.

25 In particular, a unique nucleic acid region is preferably of mammalian origin and preferably human.

A second aspect of the invention features a nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
30 SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,

SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
5 SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
10 SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
15 SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
20 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the nucleic acid  
probe encodes a kinase polypeptide that is a fragment of the protein encoded by an amino  
acid sequence selected from the group consisting of those set forth in SEQ ID NO:122,  
SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127,  
25 SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132,  
SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137,  
SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147,  
SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152,  
30 SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157,  
SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162,  
SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,

SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172,  
SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177,  
SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,  
SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,  
5 SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
10 SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
15 SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242, or the corresponding full-length amino acid sequences. The nucleic acid probe  
contains a nucleotide base sequence that will hybridize to a sequence selected from the  
group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ  
ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,  
20 SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ  
ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID  
NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25,  
SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ  
ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID  
25 NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41,  
SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ  
ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID  
NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57,  
SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ  
30 ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID  
NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73,  
SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ

ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, or a functional derivative thereof.

In preferred embodiments, the nucleic acid probe hybridizes to nucleic acid encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous amino acids of a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID

NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID  
NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID  
NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID  
NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID  
5 NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ  
ID NO:242, or the corresponding full-length amino acid sequence, or functional  
derivatives thereof.

Methods for using the probes include detecting the presence or amount of kinase  
RNA in a sample by contacting the sample with a nucleic acid probe under conditions  
10 such that hybridization occurs and detecting the presence or amount of the probe bound to  
kinase RNA. The nucleic acid duplex formed between the probe and a nucleic acid  
sequence coding for a kinase polypeptide may be used in the identification of the sequence  
of the nucleic acid detected (Nelson *et al.*, in *Nonisotopic DNA Probe Techniques*,  
Academic Press, San Diego, Kricka, ed., p. 275, 1992, hereby incorporated by reference  
15 herein in its entirety, including any drawings, figures, or tables). Kits for performing such  
methods may be constructed to include a container means having disposed therein a  
nucleic acid probe.

In a third aspect, the invention describes a recombinant cell or tissue comprising a  
nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of  
20 SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126,  
SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131,  
SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,  
SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146,  
25 SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151,  
SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156,  
SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,  
30 SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,

SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
5 SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
10 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
and SEQ ID NO:242. In such cells, the nucleic acid may be under the control of the  
genomic regulatory elements, or may be under the control of exogenous regulatory  
elements including an exogenous promoter. By "exogenous" it is meant a promoter that is  
15 not normally coupled *in vivo* transcriptionally to the coding sequence for the kinase  
polypeptides.

The polypeptide is preferably a fragment of the protein encoded by an amino acid  
sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID  
20 NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID  
NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID  
NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID  
NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID  
NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID  
25 NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID  
NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID  
NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID  
NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID  
NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID  
30 NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID  
NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID  
NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID



NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID  
NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID  
NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID  
NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID  
5 NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID  
NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID  
NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID  
NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID  
NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID  
10 NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the  
corresponding full-length amino acid sequence. By "fragment," is meant an amino acid  
sequence present in a kinase polypeptide. Preferably, such a sequence comprises at least  
10, 20, 40, 50, 75, 100, 200, or 300 contiguous amino acids a sequence selected from the  
group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
15 SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
20 SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
25 SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
30 SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,

SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
5 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or of the corresponding full-  
length amino acid sequence, or a functional derivative thereof.

In a fourth aspect, the invention features an isolated, enriched, or purified kinase  
polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ  
10 ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ  
ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ  
ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ  
ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ  
ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ  
15 ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ  
ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ  
ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ  
ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ  
ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ  
20 ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ  
ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ  
ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ  
ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ  
ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ  
25 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ  
ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ  
ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ  
ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ  
ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ  
30 ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ  
ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ

ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

By "isolated" in reference to a polypeptide is meant a polymer of amino acids (2 or more amino acids) conjugated to each other, including polypeptides that are isolated from a natural source or that are synthesized. The isolated polypeptides of the present invention are unique in the sense that they are not found in a pure or separated state in nature. Use of the term "isolated" indicates that a naturally occurring sequence has been removed from its normal cellular environment. Thus, the sequence may be in a cell-free solution or placed in a different cellular environment. The term does not imply that the sequence is the only amino acid chain present, but that it is essentially free (about 90 - 95% pure at least) of non-amino acid material naturally associated with it.

By the use of the term "enriched" in reference to a polypeptide is meant that the specific amino acid sequence constitutes a significantly higher fraction (2 - 5 fold) of the total amino acid sequences present in the cells or solution of interest than in normal or diseased cells or in the cells from which the sequence was taken. This could be caused by a person by preferential reduction in the amount of other amino acid sequences present, or by a preferential increase in the amount of the specific amino acid sequence of interest, or by a combination of the two. However, it should be noted that enriched does not imply that there are no other amino acid sequences present, just that the relative amount of the sequence of interest has been significantly increased. The term significant here is used to indicate that the level of increase is useful to the person making such an increase, and generally means an increase relative to other amino acid sequences of about at least 2-fold, more preferably at least 5- to 10-fold or even more. The term also does not imply that there is no amino acid sequence from other sources. The other source of amino acid sequences may, for example, comprise amino acid sequence encoded by a yeast or bacterial genome, or a cloning vector such as pUC19. The term is meant to cover only those situations in which man has intervened to increase the proportion of the desired amino acid sequence.

It is also advantageous for some purposes that an amino acid sequence be in purified form. The term "purified" in reference to a polypeptide does not require absolute purity (such as a homogeneous preparation); instead, it represents an indication that the sequence is relatively purer than in the natural environment. Compared to the natural level

this level should be at least 2-5 fold greater (*e.g.*, in terms of mg/mL). Purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated. The substance is preferably free of contamination at a functionally significant level, for example 90%, 95%, or 99% pure.

5           In preferred embodiments, the kinase polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,  
10       SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
15       SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
20       SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
25       SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
30       SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequences. Preferably, the kinase polypeptide contains at least 10, 20, 40, 50, 75, 100, 200, or 300 contiguous

amino acids a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or a functional derivative thereof.

In preferred embodiments, the kinase polypeptide comprises an amino acid sequence having (a) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ

ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ

5 ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ  
ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ  
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ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ  
10 ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ  
ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ  
ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ  
ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ  
ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ  
15 ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but  
not all, of a domain selected from the group consisting of an N-terminal domain, a  
catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region,  
a spacer region, an insert, and a C-terminal tail; (c) an amino acid sequence of a domain of  
a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122,  
20 SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127,  
SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132,  
SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137,  
SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147,  
25 SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152,  
SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157,  
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SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,  
SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172,  
30 SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177,  
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SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
5 SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
10 SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242 where the domain is selected from the group consisting of an N-terminal domain,  
a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich  
region, a spacer region, an insert, and a C-terminal tail; or (d) an amino acid sequence  
15 selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123,  
SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128,  
SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133,  
SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138,  
SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143,  
20 SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,  
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SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
25 SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
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30 SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,



SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
5 SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it  
lacks one or more, but not all, of the domains selected from the group consisting of a C-  
terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich  
10 region, a coiled-coil structure region, an insert, and a C-terminal tail. (The domain  
demarcations of the polypeptides of the invention are indicated in Table 2 by reference to  
the kinase domain.)

The polypeptide can be isolated from a natural source by methods well-known in  
the art. The natural source may be mammalian, preferably human, blood, semen, or tissue,  
15 and the polypeptide may be synthesized using an automated polypeptide synthesizer. The  
isolated, enriched, or purified kinase polypeptide is preferably selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
20 ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ  
ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ  
ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ  
ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ  
25 ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ  
ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ  
ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ  
ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ  
ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ  
30 ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ  
ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ  
ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ

ID NO:200, SEQ ID NO 201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO 206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO 218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242A.

In some embodiments the invention includes a recombinant kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,

SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. By "recombinant kinase polypeptide" is meant a polypeptide produced by recombinant DNA techniques such that it is distinct from a naturally occurring polypeptide either in its location (*e.g.*, present in a different cell or tissue than found in nature), purity or structure. Generally, such a recombinant polypeptide will be present in a cell in an amount different from that normally observed in nature.

In a fifth aspect, the invention features an antibody (*e.g.*, a monoclonal or polyclonal antibody) having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain or fragment where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ

ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. In preferred embodiments, the antibody binds specifically to domains of kinase polypeptides, that are defined *supra*.

By "specific binding affinity" is meant that the antibody binds to the target kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions. Antibodies or antibody fragments are polypeptides that contain regions that can bind other polypeptides. The term "specific binding affinity" describes an antibody that binds to a kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions.

The term "polyclonal" refers to antibodies that are heterogenous populations of antibody molecules derived from the sera of animals immunized with an antigen or an antigenic functional derivative thereof. For the production of polyclonal antibodies, various host animals may be immunized by injection with the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species.

"Monoclonal antibodies" are substantially homogenous populations of antibodies to a particular antigen. They may be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture. Monoclonal antibodies may be obtained by methods known to those skilled in the art (Kohler *et al.*, Nature 256:495-497, 1975, and U.S. Patent No. 4,376,110, both of which are hereby incorporated by reference herein in their entirety including any figures, tables, or drawings).

The term "antibody fragment" refers to a portion of an antibody, often the hyper variable region and portions of the surrounding heavy and light chains, that displays specific binding affinity for a particular molecule. A hyper variable region is a portion of an antibody that physically binds to the polypeptide target.

Antibodies or antibody fragments having specific binding affinity to a kinase polypeptide or domains of a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by probing the sample with the antibody under conditions suitable for kinase-antibody immunocomplex formation and detecting the presence and/or amount of the antibody conjugated to the

kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include antibodies or antibody fragments specific for the kinase as well as a conjugate of a binding partner of the antibodies or the antibodies themselves.

An antibody or antibody fragment with specific binding affinity to a kinase polypeptide of the invention can be isolated, enriched, or purified from a prokaryotic or eukaryotic organism. Routine methods known to those skilled in the art enable production of antibodies or antibody fragments, in both prokaryotic and eukaryotic organisms. Purification, enrichment, and isolation of antibodies, which are polypeptide molecules, are described above.

Antibodies having specific binding affinity to a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by contacting the sample with the antibody under conditions such that an immunocomplex forms and detecting the presence and/or amount of the antibody conjugated to the kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include a first container containing the antibody and a second container having a conjugate of a binding partner of the antibody and a label, such as, for example, a radioisotope. The diagnostic kit may also include notification of an FDA approved use and instructions therefor.

In a sixth aspect, the invention features a hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain, where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID

NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; and where the domains are defined as above. By "hybridoma" is meant an immortalized cell line that is capable of secreting an antibody, for example an antibody to a kinase of the invention. In preferred embodiments, the antibody to the kinase comprises a sequence of amino acids that is able to specifically bind a kinase polypeptide of the invention.

In a seventh aspect, the invention features a kinase polypeptide binding agent able to bind to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,

SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
5 SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
10 SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242. The binding agent is preferably a purified antibody that recognizes an epitope  
present on a kinase polypeptide of the invention. Other binding agents include molecules  
that bind to kinase polypeptides and analogous molecules that bind to a kinase  
15 polypeptide. Such binding agents may be identified by using assays that measure kinase  
binding partner activity, such as those that measure PDGFR activity.

The invention also features a method for screening for human cells containing a  
kinase polypeptide of the invention or an equivalent sequence. The method involves  
identifying the novel polypeptide in human cells using techniques that are routine and  
20 standard in the art, such as those described herein for identifying the kinases of the  
invention (*e.g.*, cloning, Southern or Northern blot analysis, in situ hybridization, PCR  
amplification, etc.).

In an eighth aspect, the invention features methods for identifying a substance that  
modulates kinase activity comprising the steps of: (a) contacting a kinase polypeptide  
25 selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
30 SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,

SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
5 SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
10 SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
15 SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 with a test substance; (b)  
measuring the activity of said polypeptide; and (c) determining whether said substance  
modulates the activity of said polypeptide.

20 The term "modulates" refers to the ability of a compound to alter the function of a  
kinase of the invention. A modulator preferably activates or inhibits the activity of a  
kinase of the invention.

The term "activates" refers to increasing the cellular activity of the kinase. The  
term inhibit refers to decreasing the cellular activity of the kinase. Kinase activity is  
25 preferably the interaction with a natural binding partner.

The term "modulates" also refers to altering the function of kinases of the  
invention by increasing or decreasing the probability that a complex forms between the  
kinase and a natural binding partner. A modulator preferably increases the probability that  
such a complex forms between the kinase and the natural binding partner, more preferably  
30 increases or decreases the probability that a complex forms between the kinase and the  
natural binding partner depending on the concentration of the compound exposed to the



kinase, and most preferably decreases the probability that a complex forms between the kinase and the natural binding partner.

The term "complex" refers to an assembly of at least two molecules bound to one another. Signal transduction complexes often contain at least two protein molecules  
5 bound to one another. For instance, a protein tyrosine receptor protein kinase, GRB2, SOS, RAF, and RAS assemble to form a signal transduction complex in response to a mitogenic ligand.

The term "natural binding partner" refers to polypeptides, lipids, small molecules, or nucleic acids that bind to kinases in cells. A change in the interaction between a kinase  
10 and a natural binding partner can manifest itself as an increased or decreased probability that the interaction forms, or an increased or decreased concentration of kinase/natural binding partner complex.

The term "contacting" as used herein refers to mixing a solution comprising the test compound with a liquid medium bathing the cells of the methods. The solution  
15 comprising the compound may also comprise another component, such as dimethyl sulfoxide (DMSO), which facilitates the uptake of the test compound or compounds into the cells of the methods. The solution comprising the test compound may be added to the medium bathing the cells by utilizing a delivery apparatus, such as a pipet-based device or syringe-based device.

In a ninth aspect, the invention features methods for identifying a substance that modulates kinase activity in a cell comprising the steps of: (a) expressing a kinase  
20 polypeptide in a cell, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,  
25 SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156,  
30 SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,

SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
5 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
10 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
15 and SEQ ID NO:242; (b) adding a test substance to said cell; and (c) monitoring a change  
in cell phenotype or the interaction between said polypeptide and a natural binding  
partner.

The term "expressing" as used herein refers to the production of kinases of the  
invention from a nucleic acid vector containing kinase genes within a cell. The nucleic  
20 acid vector is transfected into cells using well known techniques in the art as described  
herein.

In a tenth aspect, the invention provides methods for treating a disease or abnormal  
condition by administering to a patient in need of such treatment a substance that  
modulates the activity of a polypeptide selected from the group consisting of SEQ ID  
25 NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID  
NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID  
NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID  
30 NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID  
NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID  
NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID

NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the disease is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer. Also included are metabolic disorders, such as diabetes mellitus, and reproductive disorders, such as infertility.

Preferably, the disease or disorder is selected from the group consisting of rheumatoid arthritis, atherosclerosis, autoimmune disorders, and organ transplantation. Preferably the disease or disorder is selected from the group consisting of immune-related diseases and disorders, myocardial infarction, cardiomyopathies, stroke, renal failure, and oxidative stress-related neurodegenerative disorders. Most preferably, the immune-related diseases and disorders are selected from the group consisting of rheumatoid arthritis, chronic inflammatory bowel disease, chronic inflammatory pelvic disease, multiple sclerosis, asthma, osteoarthritis, psoriasis, atherosclerosis, rhinitis, autoimmunity, and organ transplantation.

Substances useful for treatment of disorders or diseases preferably show positive results in one or more in vitro assays for an activity corresponding to treatment of the disease or disorder in question. Substances that modulate the activity of the polypeptides

preferably include, but are not limited to, antisense oligonucleotides and inhibitors of protein kinases.

The term "preventing" refers to decreasing the probability that an organism contracts or develops an abnormal condition.

5 The term "treating" refers to having a therapeutic effect and at least partially alleviating or abrogating an abnormal condition in the organism.

The term "therapeutic effect" refers to the inhibition or activation factors causing or contributing to the abnormal condition. A therapeutic effect relieves to some extent one or more of the symptoms of the abnormal condition. In reference to the treatment of  
10 abnormal conditions, a therapeutic effect can refer to one or more of the following: (a) an increase in the proliferation, growth, and/or differentiation of cells; (b) inhibition (*i.e.*, slowing or stopping) of cell death; (c) inhibition of degeneration; (d) relieving to some extent one or more of the symptoms associated with the abnormal condition; and (e) enhancing the function of the affected population of cells. Compounds demonstrating  
15 efficacy against abnormal conditions can be identified as described herein.

The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation or cell survival. An abnormal condition may also include irregularities in cell cycle progression, *i.e.*, irregularities in  
20 normal cell cycle progression through mitosis and meiosis.

Abnormal cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

Abnormal differentiation conditions include, but are not limited to  
25 neurodegenerative disorders, slow wound healing rates, and slow tissue grafting healing rates.

Abnormal cell survival conditions relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the  
30 protein kinases could lead to cell immortality or premature cell death.

The term "aberration", in conjunction with the function of a kinase in a signal transduction process, refers to a kinase that is over- or under-expressed in an organism, mutated such that its catalytic activity is lower or higher than wild-type protein kinase activity, mutated such that it can no longer interact with a natural binding partner, is no longer modified by another protein kinase or protein phosphatase, or no longer interacts with a natural binding partner.

The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques, and carrier techniques.

The abnormal condition can also be prevented or treated by administering a compound to a group of cells having an aberration in a signal transduction pathway to an organism. The effect of administering a compound on organism function can then be monitored. The organism is preferably a mouse, rat, rabbit, guinea pig, or goat, more preferably a monkey or ape, and most preferably a human.

In an eleventh aspect, the invention features methods for detection the expression of a polypeptide in a sample as a diagnostic tool for diseases or disorders, wherein the method comprises the steps of: (a) contacting the sample with a nucleic acid probe which hybridizes under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ

ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the nucleic acid sequence encoding the polypeptide, fragments thereof, and the complements of the sequences and fragments; and (b) detecting the presence or amount of the probe:target region hybrid as an indication of the disease.

In preferred embodiments of the invention, the disease or disorder is selected from the group consisting of rheumatoid arthritis, atherosclerosis, autoimmune disorders, organ transplantation, myocardial infarction, cardiomyopathies, stroke, renal failure, oxidative stress-related neurodegenerative disorders, metabolic disorder including diabetes, reproductive disorders including infertility, and cancer.

The kinase "target region" is a nucleotide base sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID

NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36,  
SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ  
ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID  
NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52,  
5 SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ  
ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID  
NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68,  
SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ  
ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID  
10 NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84,  
SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ  
ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID  
NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID  
NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID  
15 NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID  
NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID  
NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID  
NO:120, and SEQ ID NO:121, or the corresponding full-length sequences, a functional  
derivative thereof, or a fragment thereof to which the nucleic acid probe will specifically  
20 hybridize. Specific hybridization indicates that in the presence of other nucleic acids the  
probe only hybridizes detectably with the kinase of the invention's target region. Putative  
target regions can be identified by methods well known in the art consisting of alignment  
and comparison of the most closely related sequences in the database.

In preferred embodiments the nucleic acid probe hybridizes to a kinase target  
25 region encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous  
amino acids of the sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID  
NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID  
NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID  
30 NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID  
NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID

NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or a functional derivative thereof. Hybridization conditions should be such that hybridization occurs only with the kinase genes in the presence of other nucleic acid molecules. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20 contiguous nucleotides. Such conditions are defined *supra*.

Hybridization conditions should be such that hybridization occurs only with the genes in the presence of other nucleic acid molecules. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having 1 or 2 mismatches out of 20 contiguous nucleotides. Such conditions are defined *supra*.

The diseases for which detection of kinase genes in a sample could be diagnostic include diseases in which kinase nucleic acid (DNA and/or RNA) is amplified in comparison to normal cells. By "amplification" is meant increased numbers of kinase



DNA or RNA in a cell compared with normal cells. In normal cells, kinases are typically found as single copy genes. In selected diseases, the chromosomal location of the kinase genes may be amplified, resulting in multiple copies of the gene, or amplification. Gene amplification can lead to amplification of kinase RNA, or kinase RNA can be amplified in the absence of kinase DNA amplification.

"Amplification" as it refers to RNA can be the detectable presence of kinase RNA in cells, since in some normal cells there is no basal expression of kinase RNA. In other normal cells, a basal level of expression of kinase exists, therefore in these cases amplification is the detection of at least 1-2-fold, and preferably more, kinase RNA, compared to the basal level.

The diseases that could be diagnosed by detection of kinase nucleic acid in a sample preferably include cancers. The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

Another aspect of the invention involves a method of agonizing (stimulating) or antagonizing a target of the invention and a natural binding partner associated activity in a mammal comprising administering to said mammal an agonist or antagonist to one of the above disclosed polypeptides in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of the protein of the present invention activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize associated functions is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein polypeptides. Some small organic molecules form a class of compounds that modulate the function of protein polypeptides. Examples of molecules that have been reported to inhibit the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published

November 26, 1992 by Maguire *et al.*), vinylene-azaindole derivatives (PCT WO 94 14808, published July 7, 1994 by Ballinari *et al.*), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny *et al.*), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow *et al.*), all of which are incorporated by reference herein, including any drawings.

Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein inhibitors only weakly inhibit function. In addition, many inhibit a variety of protein kinases and will therefore cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari *et al.*) describes hydrosoluble indolinone compounds that harbor tetralin, naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar groups including hydroxylated alkyl, phosphate, and ether substituents. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari *et al.*, all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon

& Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari *et al.* teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives, both of which are incorporated by reference herein, including any drawings.

5 Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722  
10 A1; Jones *et al.*, U.S. Patent No. 4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris  
15 *et al.*, J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.*, J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J. Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell *et al.*,  
20 Magnetic Resonance in Medicine 17:189-196 (1991); Mini *et al.*, Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece *et al.*, Cancer Research 47(11):2996-2999 (1977); Sculier *et al.*, Cancer Immunol. and Immunother. 23:A65 (1986); Sikora *et al.*, Cancer Letters 23:289-295 (1984); and Sikora *et al.*, Analytical Biochem. 172:344-355 (1988), all of which are incorporated  
25 herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle *et al.*, J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke *et al.*, J. Med. Chem. 36:425-432  
30 (1993); and Burke *et al.*, BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen et al., Clin. Exp. Immunol. 91:141-156 (1993); Anafi et al., Blood 82:12:3524-3529 (1993); Baker et al., J. Cell Sci. 102:543-555 (1992); Bilder et al., Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton et al., Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert et al., Experimental Cell Research 199:255-261 (1992); Dong et al., J. Leukocyte Biology 53:53-60 (1993); Dong et al., J. Immunol. 151(5):2717-2724 (1993); Gazit et al., J. Med. Chem. 32:2344-2352 (1989); Gazit et al., "J. Med. Chem. 36:3556-3564 (1993); Kaur et al., Anti-Cancer Drugs 5:213-222 (1994); Kaur et al., King et al., Biochem. J. 275:413-418 (1991); Kuo et al., Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992); Lyall et al., J. Biol. Chem. 264:14503-14509 (1989); Peterson et al., The Prostate 22:335-345 (1993); Pillemer et al., Int. J. Cancer 50:80-85 (1992); Posner et al., Molecular Pharmacology 45:673-683 (1993); Rendu et al., Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring et al., J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda et al., Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996, incorporated herein by reference in its entirety, including any drawings.

#### Methods of Treating a Disease (Enablement - i.e., Dosing)

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be

formulated in animal models to achieve a circulating concentration range that initially takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors and major organs can also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows:

- 1) the compound is administered to mice (an untreated control mouse should also be used);
- 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and
- 3) the samples are analyzed for red and white blood cell counts, blood cell composition and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness or toxicity. Gross abnormalities in tissue are noted and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5 Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

In a final aspect, the invention features a method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein the method comprises: (a) comparing a nucleic acid target region encoding the kinase polypeptide in  
10 a sample, where the kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID  
15 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID  
20 NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID

NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding the kinase polypeptide, or one or more fragments thereof; and (b) detecting  
5 differences in sequence or amount between the target region and the control target region, as an indication of the disease or disorder. Preferably, the disease or disorder is selected from the group consisting of immune-related diseases and disorders, organ transplantation, myocardial infarction, cardiovascular disease, stroke, renal failure, oxidative stress-related neurodegenerative disorders, and cancer. Immune-related diseases and disorders include,  
10 but are not limited to, those discussed previously.

The term "comparing" as used herein refers to identifying discrepancies between the nucleic acid target region isolated from a sample, and the control nucleic acid target region. The discrepancies can be in the nucleotide sequences, *e.g.* insertions, deletions, or point mutations, or in the amount of a given nucleotide sequence. Methods to determine  
15 these discrepancies in sequences are well-known to one of ordinary skill in the art. The "control" nucleic acid target region refers to the sequence or amount of the sequence found in normal cells, *e.g.* cells that are not diseased as discussed previously.

The term also includes anti-sense molecules drawn thereto.

The invention has been described broadly and generically herein. Each of the  
20 narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. For example, in some instances the nucleotide sequence of particular kinase polypeptides may not be part of a preferred  
25 embodiment.

The summary of the invention described above is not limiting and other features and advantages of the invention will be apparent from the following detailed description of the invention, and from the claims.

BRIEF DESCRIPTION OF THE FIGURES

Figures 1A to 1BB shows the amino acid sequences of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

Figures 2A to 2MMMM shows the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID



NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34,  
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ  
ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID  
NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50,  
5 SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ  
ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID  
NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66,  
SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ  
ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID  
10 NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82,  
SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ  
ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID  
NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98,  
SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103,  
15 SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108,  
SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113,  
SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118,  
SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121.

## DETAILED DESCRIPTION OF THE INVENTION

The present invention relates in part to kinase polypeptides, nucleic acids encoding  
such polypeptides, cells containing such nucleic acids, antibodies to such polypeptides,  
assays utilizing such polypeptides, and methods relating to all of the foregoing. The  
present invention is based upon the isolation and characterization of new kinase  
25 polypeptides. The polypeptides and nucleic acids may be produced using well-known and  
standard synthesis techniques when given the sequences presented herein.

### I. The Nucleic Acids of the Invention

Included within the scope of this invention are the functional equivalents of the  
30 herein-described isolated nucleic acid molecules. The degeneracy of the genetic code  
permits substitution of certain codons by other codons that specify the same amino acid  
and hence would give rise to the same protein. The nucleic acid sequence can vary

substantially since, with the exception of methionine and tryptophan, the known amino acids can be coded for by more than one codon. Thus, portions or all of the kinase genes of the invention could be synthesized to give a nucleic acid sequence significantly different from one selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121. The encoded amino acid sequence thereof would, however, be preserved.

In addition, the nucleic acid sequence may comprise a nucleotide sequence which results from the addition, deletion or substitution of at least one nucleotide to the 5'-end and/or the 3'-end of the nucleic acid sequence shown in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID

NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a derivative thereof. Any nucleotide or polynucleotide may be used in this regard, provided that its addition, deletion or substitution does not alter the amino acid sequence of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163,

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SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,  
SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178,  
SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183,  
5 SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188,  
SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193,  
SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198,  
SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,  
10 SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213,  
SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218,  
SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223,  
SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228,  
SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233,  
15 SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238,  
SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, that is encoded  
by the nucleotide sequence. For example, the present invention is intended to include any  
nucleic acid sequence resulting from the addition of ATG as an initiation codon at the 5'-  
end of the inventive nucleic acid sequence or its derivative, or from the addition of TTA,  
20 TAG or TGA as a termination codon at the 3'-end of the inventive nucleotide sequence or  
its derivative. Moreover, the nucleic acid molecule of the present invention may, as  
necessary, have restriction endonuclease recognition sites added to its 5'-end and/or 3'-  
end.

Such functional alterations of a given nucleic acid sequence afford an opportunity  
25 to promote secretion and/or processing of heterologous proteins encoded by foreign  
nucleic acid sequences fused thereto, for example. All variations of the nucleotide  
sequence of the kinase genes of the invention and fragments thereof permitted by the  
genetic code are, therefore, included in this invention.

Further, it is possible to delete codons or to substitute one or more codons with  
30 codons other than degenerate codons to produce a structurally modified polypeptide, but  
one which has substantially the same utility or activity as the polypeptide produced by the  
unmodified nucleic acid molecule. As recognized in the art, the two polypeptides are

functionally equivalent, as are the two nucleic acid molecules that give rise to their production, even though the differences between the nucleic acid molecules are not related to the degeneracy of the genetic code. This is discussed further in the "Functional Derivatives" section, herein.

5           Finally, many of the nucleic acid molecules of the invention are provided as a partial sequence only (Fig. 2A through 2QQ). However, it is standard for one of ordinary skill in the art to obtain a full-length sequence when provided with a partial sequence. Similarly, when provided with a partial or full-length sequence it is standard for one of ordinary skill in the art to obtain nucleic acid sequence coding for homologous proteins.  
10          Therefore, these nucleic acid molecules are also part of the invention.

          The characteristics of the protein kinase nucleic acid sequences of the invention are provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI, CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant number of protein kinases that do not belong to any of the known groups, and therefore  
15          presumably define new protein kinase groups.

          Additional characteristics may be found, *inter alia*, in the tables, namely Table 1, Table 2, Table 3 and Table 4, shown below.

## 20          II.       Nucleic Acid Probes, Methods, and Kits for Detection of Protein Kinases.

          A nucleic acid probe of the present invention may be used to probe an appropriate chromosomal or cDNA library by usual hybridization methods to obtain other nucleic acid molecules of the present invention. A chromosomal DNA or cDNA library may be prepared from appropriate cells according to recognized methods in the art (cf. "Molecular Cloning: A Laboratory Manual", second edition, Cold Spring Harbor Laboratory,  
25          Sambrook, Fritsch, & Maniatis, eds., 1989).

          In the alternative, chemical synthesis can be carried out in order to obtain nucleic acid probes having nucleotide sequences that correspond to N-terminal, kinase or C-terminal portions, for example, of the amino acid sequence of the polypeptide of interest. The synthesized nucleic acid probes may be used as primers in a polymerase chain  
30          reaction (PCR) carried out in accordance with recognized PCR techniques, essentially according to PCR Protocols, "A Guide to Methods and Applications", Academic Press.

Michael, *et al.*, eds., 1990, utilizing the appropriate chromosomal or cDNA library to obtain the fragment of the present invention.

One skilled in the art can readily design such probes based on the sequence disclosed herein using methods of computer alignment and sequence analysis known in the art ("Molecular Cloning: A Laboratory Manual", 1989, *supra*). The hybridization probes of the present invention can be labeled by standard labeling techniques such as with a radiolabel, enzyme label, fluorescent label, biotin-avidin label, chemiluminescence, and the like. After hybridization, the probes may be visualized using known methods.

The nucleic acid probes of the present invention include RNA, as well as DNA probes, such probes being generated using techniques known in the art. The nucleic acid probe may be immobilized on a solid support. Examples of such solid supports include, but are not limited to, plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, and acrylic resins, such as polyacrylamide and latex beads. Techniques for coupling nucleic acid probes to such solid supports are well known in the art.

The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

One method of detecting the presence of nucleic acids of the invention in a sample comprises (a) contacting said sample with the above-described nucleic acid probe under conditions such that hybridization occurs, and (b) detecting the presence of said probe bound to said nucleic acid molecule. One skilled in the art would select the nucleic acid probe according to techniques known in the art as described above. Samples to be tested include but should not be limited to RNA samples of human tissue.

A kit for detecting the presence of nucleic acids of the invention in a sample comprises at least one container means having disposed therein the above-described nucleic acid probe. The kit may further comprise other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound nucleic acid probe. Examples of detection reagents include, but are not limited to

radiolabelled probes, enzymatic labeled probes (horseradish peroxidase, alkaline phosphatase), and affinity labeled probes (biotin, avidin, or streptavidin).

In detail, a compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers  
5 or strips of plastic or paper. Such containers allow the efficient transfer of reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the probe or  
10 primers used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, and the like), and containers which contain the reagents used to detect the hybridized probe, bound antibody, amplified product, or the like. One skilled in the art will readily recognize that the nucleic acid probes described in the present invention can readily be incorporated into one of the established kit formats that are well  
15 known in the art.

### III. DNA Constructs Comprising a Protein Kinase Nucleic Acid Molecule and Cells Containing These Constructs.

The present invention also relates to a recombinant DNA molecule comprising, 5' to 3', a promoter effective to initiate transcription in a host cell and the above-described nucleic acid molecules. In addition, the present invention relates to a recombinant DNA molecule comprising a vector and an above-described nucleic acid molecule. The present invention also relates to a nucleic acid molecule comprising a transcriptional region functional in a cell, a sequence complementary to an RNA sequence encoding an amino  
20 acid sequence corresponding to the above-described polypeptide, and a transcriptional termination region functional in said cell. The above-described molecules may be isolated and/or purified DNA molecules.

The present invention also relates to a cell or organism that contains an above-described nucleic acid molecule and thereby is capable of expressing a polypeptide. The polypeptide may be purified from cells that have been altered to express the polypeptide.  
30 A cell is said to be "altered to express a desired polypeptide" when the cell, through genetic manipulation, is made to produce a protein which it normally does not produce or

which the cell normally produces at lower levels. One skilled in the art can readily adapt procedures for introducing and expressing either genomic, cDNA, or synthetic sequences into either eukaryotic or prokaryotic cells.

5 A nucleic acid molecule, such as DNA, is said to be "capable of expressing" a polypeptide if it contains nucleotide sequences which contain transcriptional and translational regulatory information and such sequences are "operably linked" to nucleotide sequences which encode the polypeptide. An operable linkage is a linkage in which the regulatory DNA sequences and the DNA sequence sought to be expressed are connected in such a way as to permit gene sequence expression. The precise nature of the regulatory regions needed for gene sequence expression may vary from organism to organism, but shall in general include a promoter region which, in prokaryotes, contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

10 If desired, the non-coding region 3' to the sequence encoding a kinase of the invention may be obtained by the above-described methods. This region may be retained for its transcriptional termination regulatory sequences, such as termination and polyadenylation. Thus, by retaining the 3'-region naturally contiguous to the DNA sequence encoding a kinase of the invention, the transcriptional termination signals may be provided. Where the transcriptional termination signals are not satisfactorily functional in the expression host cell, then a 3' region functional in the host cell may be substituted.

20 Two DNA sequences (such as a promoter region sequence and a sequence encoding a kinase of the invention) are said to be operably linked if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region sequence to direct the transcription of a gene sequence encoding a kinase of the invention, or (3) interfere with the ability of the gene sequence of a kinase of the invention to be transcribed by the promoter region sequence. Thus, a promoter region would be operably linked to a DNA sequence if the promoter were capable of effecting transcription of that DNA sequence.



Thus, to express a gene encoding a kinase of the invention, transcriptional and translational signals recognized by an appropriate host are necessary.

The present invention encompasses the expression of a gene encoding a kinase of the invention (or a functional derivative thereof) in either prokaryotic or eukaryotic cells. Prokaryotic hosts are, generally, very efficient and convenient for the production of recombinant proteins and are, therefore, one type of preferred expression system for kinases of the invention. Prokaryotes most frequently are represented by various strains of *E. coli*. However, other microbial strains may also be used, including other bacterial strains.

In prokaryotic systems, plasmid vectors that contain replication sites and control sequences derived from a species compatible with the host may be used. Examples of suitable plasmid vectors may include pBR322, pUC118, pUC119 and the like; suitable phage or bacteriophage vectors may include  $\gamma$ gt10,  $\gamma$ gt11 and the like; and suitable virus vectors may include pMAM-neo, pKRC and the like. Preferably, the selected vector of the present invention has the capacity to replicate in the selected host cell.

Recognized prokaryotic hosts include bacteria such as *E. coli*, *Bacillus*, *Streptomyces*, *Pseudomonas*, *Salmonella*, *Serratia*, and the like. However, under such conditions, the polypeptide will not be glycosylated. The prokaryotic host must be compatible with the replicon and control sequences in the expression plasmid.

To express a kinase of the invention (or a functional derivative thereof) in a prokaryotic cell, it is necessary to operably link the sequence encoding the kinase of the invention to a functional prokaryotic promoter. Such promoters may be either constitutive or, more preferably, regulatable (*i.e.*, inducible or derepressible). Examples of constitutive promoters include the *int* promoter of bacteriophage  $\lambda$ , the *bla* promoter of the  $\beta$ -lactamase gene sequence of pBR322, and the *cat* promoter of the chloramphenicol acetyl transferase gene sequence of pPR325, and the like. Examples of inducible prokaryotic promoters include the major right and left promoters of bacteriophage  $\lambda$  ( $P_L$  and  $P_R$ ), the *trp*, *recA*, *lacZ*, *lacI*, and *gal* promoters of *E. coli*, the  $\alpha$ -amylase (Ulmanen *et al.*, J. Bacteriol. 162:176-182, 1985) and the  $\zeta$ -28-specific promoters of *B. subtilis* (Gilman *et al.*, Gene Sequence 32:11-20, 1984), the promoters of the bacteriophages of *Bacillus* (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, Inc., NY, 1982), and *Streptomyces* promoters (Ward *et al.*, Mol. Gen. Genet. 203:468-478, 1986). Prokaryotic

promoters are reviewed by Glick (Ind. Microbiol. 1:277-282, 1987), Ceniatiempo (Biochimie 68:505-516, 1986), and Gottesman (Ann. Rev. Genet. 18:415-442, 1984).

Proper expression in a prokaryotic cell also requires the presence of a ribosome-binding site upstream of the gene sequence-encoding sequence. Such ribosome-binding sites are disclosed, for example, by Gold *et al.* (Ann. Rev. Microbiol. 35:365-404, 1981). The selection of control sequences, expression vectors, transformation methods, and the like, are dependent on the type of host cell used to express the gene. As used herein, "cell", "cell line", and "cell culture" may be used interchangeably and all such designations include progeny. Thus, the words "transformants" or "transformed cells" include the primary subject cell and cultures derived therefrom, without regard to the number of transfers. It is also understood that all progeny may not be precisely identical in DNA content, due to deliberate or inadvertent mutations. However, as defined, mutant progeny have the same functionality as that of the originally transformed cell.

Host cells which may be used in the expression systems of the present invention are not strictly limited, provided that they are suitable for use in the expression of the kinase polypeptide of interest. Suitable hosts may often include eukaryotic cells. Preferred eukaryotic hosts include, for example, yeast, fungi, insect cells, mammalian cells either *in vivo*, or in tissue culture. Mammalian cells which may be useful as hosts include HeLa cells, cells of fibroblast origin such as VERO or CHO-K1, or cells of lymphoid origin and their derivatives. Preferred mammalian host cells include SP2/0 and J558L, as well as neuroblastoma cell lines such as IMR 332, which may provide better capacities for correct post-translational processing.

In addition, plant cells are also available as hosts, and control sequences compatible with plant cells are available, such as the cauliflower mosaic virus 35S and 19S, and nopaline synthase promoter and polyadenylation signal sequences. Another preferred host is an insect cell, for example the *Drosophila* larvae. Using insect cells as hosts, the *Drosophila* alcohol dehydrogenase promoter can be used (Rubin, Science 240:1453-1459, 1988). Alternatively, baculovirus vectors can be engineered to express large amounts of kinases of the invention in insect cells (Jasny, Science 238:1653, 1987; Miller *et al.*, In: Genetic Engineering, Vol. 8, Plenum, Setlow *et al.*, eds., pp. 277-297, 1986).

Any of a series of yeast expression systems can be utilized which incorporate promoter and termination elements from the actively expressed sequences coding for glycolytic enzymes that are produced in large quantities when yeast are grown in mediums rich in glucose. Known glycolytic gene sequences can also provide very efficient transcriptional control signals. Yeast provides substantial advantages in that it can also carry out post-translational modifications. A number of recombinant DNA strategies exist utilizing strong promoter sequences and high copy number plasmids which can be utilized for production of the desired proteins in yeast. Yeast recognizes leader sequences on cloned mammalian genes and secretes peptides bearing leader sequences (*i.e.*, pre-peptides). Several possible vector systems are available for the expression of kinases of the invention in a mammalian host.

A wide variety of transcriptional and translational regulatory sequences may be employed, depending upon the nature of the host. The transcriptional and translational regulatory signals may be derived from viral sources, such as adenovirus, bovine papilloma virus, cytomegalovirus, simian virus, or the like, where the regulatory signals are associated with a particular gene sequence which has a high level of expression. Alternatively, promoters from mammalian expression products, such as actin, collagen, myosin, and the like, may be employed. Transcriptional initiation regulatory signals may be selected which allow for repression or activation, so that expression of the gene sequences can be modulated. Of interest are regulatory signals which are temperature-sensitive so that by varying the temperature, expression can be repressed or initiated, or are subject to chemical (such as metabolite) regulation.

Expression of kinases of the invention in eukaryotic hosts requires the use of eukaryotic regulatory regions. Such regions will, in general, include a promoter region sufficient to direct the initiation of RNA synthesis. Preferred eukaryotic promoters include, for example, the promoter of the mouse metallothionein I gene sequence (Hamer *et al.*, J. Mol. Appl. Gen. 1:273-288, 1982); the TK promoter of Herpes virus (McKnight, Cell 31:355-365, 1982); the SV40 early promoter (Benoist *et al.*, Nature (London) 290:304-31, 1981); and the yeast gal4 gene sequence promoter (Johnston *et al.*, Proc. Natl. Acad. Sci. (USA) 79:6971-6975, 1982; Silver *et al.*, Proc. Natl. Acad. Sci. (USA) 81:5951-5955, 1984).

Translation of eukaryotic mRNA is initiated at the codon that encodes the first methionine. For this reason, it is preferable to ensure that the linkage between a eukaryotic promoter and a DNA sequence which encodes a kinase of the invention (or a functional derivative thereof) does not contain any intervening codons which are capable of encoding a methionine (*i.e.*, AUG). The presence of such codons results either in the formation of a fusion protein (if the AUG codon is in the same reading frame as the kinase of the invention coding sequence) or a frame-shift mutation (if the AUG codon is not in the same reading frame as the kinase of the invention coding sequence).

A nucleic acid molecule encoding a kinase of the invention and an operably linked promoter may be introduced into a recipient prokaryotic or eukaryotic cell either as a nonreplicating DNA or RNA molecule, which may either be a linear molecule or, more preferably, a closed covalent circular molecule. Since such molecules are incapable of autonomous replication, the expression of the gene may occur through the transient expression of the introduced sequence. Alternatively, permanent expression may occur through the integration of the introduced DNA sequence into the host chromosome.

A vector may be employed which is capable of integrating the desired gene sequences into the host cell chromosome. Cells which have stably integrated the introduced DNA into their chromosomes can be selected by also introducing one or more markers which allow for selection of host cells which contain the expression vector. The marker may provide for prototrophy to an auxotrophic host, biocide resistance, *e.g.*, antibiotics, or heavy metals, such as copper, or the like. The selectable marker gene sequence can either be directly linked to the DNA gene sequences to be expressed, or introduced into the same cell by co-transfection. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcription promoters, enhancers, and termination signals. cDNA expression vectors incorporating such elements include those described by Okayama (Mol. Cell. Biol. 3:280-, 1983).

The introduced nucleic acid molecule can be incorporated into a plasmid or viral vector capable of autonomous replication in the recipient host. Any of a wide variety of vectors may be employed for this purpose. Factors of importance in selecting a particular plasmid or viral vector include: the ease with which recipient cells that contain the vector may be recognized and selected from those recipient cells which do not contain the vector;

the number of copies of the vector which are desired in a particular host; and whether it is desirable to be able to "shuttle" the vector between host cells of different species.

Preferred prokaryotic vectors include plasmids such as those capable of replication in *E. coli* (such as, for example, pBR322, ColEI, pSC101, pACYC 184,  $\pi$ VX; "Molecular Cloning: A Laboratory Manual", 1989, *supra*). *Bacillus* plasmids include pC194, pC221, pT127, and the like (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, NY, pp. 307-329, 1982). Suitable *Streptomyces* plasmids include pIJ101 (Kendall *et al.*, J. Bacteriol. 169:4177-4183, 1987), and streptomyces bacteriophages such as  $\phi$ C31 (Chater *et al.*, In: Sixth International Symposium on Actinomycetales Biology, Akademiai Kiado, Budapest, Hungary, pp. 45-54, 1986). *Pseudomonas* plasmids are reviewed by John *et al.* (Rev. Infect. Dis. 8:693-704, 1986), and Izaki (Jpn. J. Bacteriol. 33:729-742, 1978).

Preferred eukaryotic plasmids include, for example, BPV, vaccinia, SV40, 2-micron circle, and the like, or their derivatives. Such plasmids are well known in the art (Botstein *et al.*, Miami Wntr. Symp. 19:265-274, 1982; Broach, In: "The Molecular Biology of the Yeast *Saccharomyces*: Life Cycle and Inheritance", Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, p. 445-470, 1981; Broach, Cell 28:203-204, 1982; Bollon *et al.*, J. Clin. Hematol. Oncol. 10:39-48, 1980; Maniatis, In: Cell Biology: A Comprehensive Treatise, Vol. 3, Gene Sequence Expression, Academic Press, NY, pp. 563-608, 1980).

Once the vector or nucleic acid molecule containing the construct(s) has been prepared for expression, the DNA construct(s) may be introduced into an appropriate host cell by any of a variety of suitable means, *i.e.*, transformation, transfection, conjugation, protoplast fusion, electroporation, particle gun technology, calcium phosphate-precipitation, direct microinjection, and the like. After the introduction of the vector, recipient cells are grown in a selective medium, which selects for the growth of vector-containing cells. Expression of the cloned gene(s) results in the production of a kinase of the invention, or fragments thereof. This can take place in the transformed cells as such, or following the induction of these cells to differentiate (for example, by administration of bromodeoxyuracil to neuroblastoma cells or the like). A variety of incubation conditions can be used to form the peptide of the present invention. The most preferred conditions are those which mimic physiological conditions.

#### IV. The Proteins of the Invention

A variety of methodologies known in the art can be utilized to obtain the polypeptides of the present invention. The polypeptides may be purified from tissues or cells that naturally produce the polypeptides. Alternatively, the above-described isolated  
5 nucleic acid fragments could be used to express the kinases of the invention in any organism. The samples of the present invention include cells, protein extracts or membrane extracts of cells, or biological fluids. The samples will vary based on the assay format, the detection method, and the nature of the tissues, cells or extracts used as the sample.

10 Any eukaryotic organism can be used as a source for the polypeptides of the invention, as long as the source organism naturally contains such polypeptides. As used herein, "source organism" refers to the original organism from which the amino acid sequence of the subunit is derived, regardless of the organism the subunit is expressed in and ultimately isolated from.

15 One skilled in the art can readily follow known methods for isolating proteins in order to obtain the polypeptides free of natural contaminants. These include, but are not limited to: size-exclusion chromatography, HPLC, ion-exchange chromatography, and immuno-affinity chromatography.

Further, the polypeptides of the invention include the full-length polypeptides that  
20 can be identified from the full-length or partial sequences encoded by SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142,  
25 SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167,  
30 SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,

SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,  
SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199,  
SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197,  
SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202,  
5 SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207,  
SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212,  
SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222,  
SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227,  
10 SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232,  
SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237,  
SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID  
NO:242 (Figure 1). In addition, the polypeptides of the invention include the domains of  
these polypeptides, including, but not limited to, the N-terminal, kinase/catalytic, and C-  
15 terminal domains.

The characteristics of the protein kinase nucleic acid sequences of the invention are  
provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI,  
CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant  
number of protein kinases that do not belong to any of the known groups, and therefore  
20 presumably define new protein kinase groups.

Additional characteristics are shown in, *inter alia*, the tables, namely Table 1,  
Table 2, Table 3 and Table 4, provided below.

#### V. Antibodies, Hybridomas, Methods of Use and Kits for Detection of Protein 25 Kinases

The present invention relates to an antibody having binding affinity to a kinase of  
the invention. The polypeptide may have an amino acid sequence selected from the group  
consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ  
ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ  
30 ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ  
ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ  
ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or a functional derivative thereof, or at least 9 contiguous amino acids thereof (preferably, at least 20, 30, 35, or 40 or more contiguous amino acids thereof). Alternatively, the antibody may bind to a part of the polypeptide not provided in the sequences above, but that is present in the full-length sequence of the polypeptide and that is easily obtained using methods standard in the art. Further, the antibody may bind specifically to particular domains of one or more of the kinases of the invention, including, but not limited to, the N-terminal, kinase/catalytic, or C-terminal domains.

The present invention also relates to an antibody having specific binding affinity to a kinase or kinase domain of the invention. Such an antibody may be isolated by comparing its binding affinity to a kinase of the invention with its binding affinity to other polypeptides. Those that bind selectively to a kinase of the invention would be chosen for use in methods requiring a distinction between a kinase of the invention and other



polypeptides. Such methods could include, but should not be limited to, the analysis of altered kinase expression in tissue containing other polypeptides.

The kinases of the present invention can be used in a variety of procedures and methods, such as for the generation of antibodies, for use in identifying pharmaceutical compositions, and for studying DNA/protein interaction.

The kinases of the present invention can be used to produce antibodies or hybridomas. One skilled in the art will recognize that if an antibody is desired, such a peptide could be generated as described herein and used as an immunogen. The antibodies of the present invention include monoclonal and polyclonal antibodies, as well fragments of these antibodies, and humanized forms. Humanized forms of the antibodies of the present invention may be generated using one of the procedures known in the art such as chimerization or CDR grafting.

The present invention also relates to a hybridoma that produces the above-described monoclonal antibody, or binding fragment thereof. A hybridoma is an immortalized cell line that is capable of secreting a specific monoclonal antibody.

In general, techniques for preparing monoclonal antibodies and hybridomas are well known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1984; St. Groth *et al.*, J. Immunol. Methods 35:1-21, 1980). Any animal (mouse, rabbit, and the like) which is known to produce antibodies can be immunized with the selected polypeptide. Methods for immunization are well known in the art. Such methods include subcutaneous or intraperitoneal injection of the polypeptide. One skilled in the art will recognize that the amount of polypeptide used for immunization will vary based on the animal that is immunized, the antigenicity of the polypeptide and the site of injection.

The polypeptide may be modified or administered in an adjuvant in order to increase the peptide antigenicity. Methods of increasing the antigenicity of a polypeptide are well known in the art. Such procedures include coupling the antigen with a heterologous protein (such as globulin or  $\beta$ -galactosidase) or through the inclusion of an adjuvant during immunization.

For monoclonal antibodies, spleen cells from the immunized animals are removed, fused with myeloma cells, such as SP2'O-Agl4 myeloma cells, and allowed to become monoclonal antibody producing hybridoma cells. Any one of a number of methods well known in the art can be used to identify the hybridoma cell that produces an antibody with the desired characteristics. These include screening the hybridomas with an ELISA assay, western blot analysis, or radioimmunoassay (Lutz *et al.*, Exp. Cell Res. 175:109-124, 1988). Hybridomas secreting the desired antibodies are cloned and the class and subclass are determined using procedures known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology", *supra*, 1984).

For polyclonal antibodies, antibody-containing antisera is isolated from the immunized animal and is screened for the presence of antibodies with the desired specificity using one of the above-described procedures. The above-described antibodies may be detectably labeled. Antibodies can be detectably labeled through the use of radioisotopes, affinity labels (such as biotin, avidin, and the like), enzymatic labels (such as horse radish peroxidase, alkaline phosphatase, and the like) fluorescent labels (such as FITC or rhodamine, and the like), paramagnetic atoms, and the like. Procedures for accomplishing such labeling are well-known in the art, for example, *see* Stemberger *et al.*, J. Histochem. Cytochem. 18:315, 1970; Bayer *et al.*, Meth. Enzym. 62:308-, 1979; Engval *et al.*, Immunol. 109:129-, 1972; Goding, J. Immunol. Meth. 13:215-, 1976. The labeled antibodies of the present invention can be used for *in vitro*, *in vivo*, and *in situ* assays to identify cells or tissues that express a specific peptide.

The above-described antibodies may also be immobilized on a solid support. Examples of such solid supports include plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, acrylic resins and such as polyacrylamide and latex beads. Techniques for coupling antibodies to such solid supports are well known in the art (Weir *et al.*, "Handbook of Experimental Immunology" 4th Ed., Blackwell Scientific Publications, Oxford, England, Chapter 10, 1986; Jacoby *et al.*, Meth. Enzym. 34, Academic Press, N.Y., 1974). The immobilized antibodies of the present invention can be used for *in vitro*, *in vivo*, and *in situ* assays as well as in immunochromatography.

Furthermore, one skilled in the art can readily adapt currently available procedures, as well as the techniques, methods and kits disclosed herein with regard to antibodies, to generate peptides capable of binding to a specific peptide sequence in order to generate rationally designed antipeptide peptides (Hurby *et al.*, "Application of Synthetic Peptides: Antisense Peptides", In Synthetic Peptides, A User's Guide, W.H. Freeman, NY, pp. 289-307, 1992; Kaspczak *et al.*, Biochemistry 28:9230-9238, 1989).

Anti-peptide peptides can be generated by replacing the basic amino acid residues found in the peptide sequences of the kinases of the invention with acidic residues, while maintaining hydrophobic and uncharged polar groups. For example, lysine, arginine, and/or histidine residues are replaced with aspartic acid or glutamic acid and glutamic acid residues are replaced by lysine, arginine or histidine.

The present invention also encompasses a method of detecting a kinase polypeptide in a sample, comprising: (a) contacting the sample with an above-described antibody, under conditions such that immunocomplexes form, and (b) detecting the presence of said antibody bound to the polypeptide. In detail, the methods comprise incubating a test sample with one or more of the antibodies of the present invention and assaying whether the antibody binds to the test sample. Altered levels of a kinase of the invention in a sample as compared to normal levels may indicate disease.

Conditions for incubating an antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the antibody used in the assay. One skilled in the art will recognize that any one of the commonly available immunological assay formats (such as radioimmunoassays, enzyme-linked immunosorbent assays, diffusion based Ouchterlony, or rocket immunofluorescent assays) can readily be adapted to employ the antibodies of the present invention. Examples of such assays can be found in Chard ("An Introduction to Radioimmunoassay and Related Techniques" Elsevier Science Publishers, Amsterdam, The Netherlands, 1986), Bullock *et al.* ("Techniques in Immunocytochemistry," Academic Press, Orlando, FL Vol. 1, 1982; Vol. 2, 1983; Vol. 3, 1985), Tijssen ("Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1985).

The immunological assay test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as blood, serum, plasma, or urine. The test samples used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is testable with the system utilized.

A kit contains all the necessary reagents to carry out the previously described methods of detection. The kit may comprise: (i) a first container means containing an above-described antibody, and (ii) second container means containing a conjugate comprising a binding partner of the antibody and a label. In another preferred embodiment, the kit further comprises one or more other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound antibodies.

Examples of detection reagents include, but are not limited to, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the chromophoric, enzymatic, or antibody binding reagents that are capable of reacting with the labeled antibody. The compartmentalized kit may be as described above for nucleic acid probe kits. One skilled in the art will readily recognize that the antibodies described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

#### VI. Isolation of Compounds That Interact With Protein Kinases

The present invention also relates to a method of detecting a compound capable of binding to a protein kinase of the invention, comprising incubating the compound with a kinase of the invention and detecting the presence of the compound bound to the kinase. The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts.

The present invention also relates to a method of detecting an agonist or antagonist of kinase activity or kinase binding partner activity comprising incubating cells that produce a kinase of the invention in the presence of a compound and detecting changes in the level of kinase activity or kinase binding partner activity. The compounds thus identified would produce a change in activity indicative of the presence of the compound.

The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts. Once the compound is identified it can be isolated using techniques well known in the art.

5 The present invention also encompasses a method of agonizing (stimulating) or antagonizing kinase associated activity in a mammal comprising administering to said mammal an agonist or antagonist to a kinase of the invention in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of kinase activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize kinase associated functions  
10 is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein kinases. Some small organic molecules form a class of compounds that modulate the function of protein kinases. Examples of molecules that have been reported to inhibit  
15 the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published November 26, 1992 by Maguire *et al.*), vinylene-azaindole derivatives (PCT WO 94/14808, published July 7, 1994 by Ballinari *et al.*), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1),  
20 seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny *et al.*), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow *et al.*).

25 Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein kinase inhibitors only weakly inhibit the function of protein kinases. In addition, many inhibit a variety of protein kinases and will cause multiple side-effects as therapeutics for diseases.

30 Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari *et al.*) describes hydrosoluble indolinone compounds that harbor tetralin,

naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar moieties including hydroxylated alkyl, phosphate, and ether moieties. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari *et al.*, all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang *et al.* (Lyon & Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari *et al.* teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives.

Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722 A1; Jones *et al.*, U.S. Patent No. 4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris *et al.*, J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.*, J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J.

Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell *et al.*, Magnetic Resonance in Medicine 17:189-196 (1991); Mini *et al.*, Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece *et al.*, Cancer Research 47(11):2996-2999 (1977); Sculier *et al.*, Cancer Immunol. and Immunother. 23:A65 (1986); Sikora *et al.*, Cancer Letters 23:289-295 (1984); Sikora *et al.*, Analytical Biochem. 172:344-355 (1988); all of which are incorporated herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle *et al.*, J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke *et al.*, J. Med. Chem. 36:425-432 (1993); and Burke *et al.*, BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen *et al.*, Clin. Exp. Immunol. 91:141-156 (1993); Anafi *et al.*, Blood 82:12:3524-3529 (1993); Baker *et al.*, J. Cell Sci. 102:543-555 (1992); Bilder *et al.*, Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton *et al.*, Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert *et al.*, Experimental Cell Research 199:255-261 (1992); Dong *et al.*, J. Leukocyte Biology 53:53-60 (1993); Dong *et al.*, J. Immunol. 151(5):2717-2724 (1993); Gazit *et al.*, J. Med. Chem. 32:2344-2352 (1989); Gazit *et al.*, " J. Med. Chem. 36:3556-3564 (1993); Kaur *et al.*, Anti-Cancer Drugs 5:213-222 (1994); Kaur *et al.*, King *et al.*, Biochem. J. 275:413-418 (1991); Kuo *et al.*, Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992); Lyall *et al.*, J. Biol. Chem. 264:14503-14509 (1989); Peterson *et al.*, The Prostate 22:335-345 (1993); Pillemer *et al.*, Int. J. Cancer 50:80-85 (1992); Posner *et al.*, Molecular Pharmacology 45:673-683 (1993); Rendu *et al.*, Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring *et al.*, J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda *et al.*, Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996, incorporated herein by reference in its entirety, including any drawings.

VII. Biological Significance, Applications and Clinical Relevance of Novel Protein  
5 Kinases

For each protein kinase in this application, we provide a classification of the protein class and family to which it belongs, a summary of non-catalytic protein motifs, a profile of its expression in several hundred tissue and cell sources, and a chromosomal location. This information can be used to suggest potential function, regulation or  
10 therapeutic utility for each of the proteins.

The kinase classification and protein domains often reflect pathways, cellular roles, or mechanisms of up- or down-stream regulation. Also disease-relevant genes often occur in families of related genes. For example if one member of a kinase family functions as an oncogene, a tumor suppressor, or has been found to be disrupted in an immune,  
15 neurologic, cardiovascular, or metabolic disorder, frequently other family members may play a related role.

The expression analysis organizes kinases into groups that are transcriptionally upregulated in tumors and those that are more restricted to specific tumor types such as melanoma or prostate. This analysis also identifies genes that are regulated in a cell cycle  
20 dependent manner, and are therefore likely to be involved in maintaining cell cycle checkpoints, entry, progression, or exit from mitosis, oversee DNA repair, or are involved in cell proliferation and genome stability. Expression data also can identify genes expressed in endothelial sources or other tissues that suggest a role in angiogenesis, thereby implicating them as targets for control of diseases that have an angiogenic  
25 component, such as cancer, endometriosis, retinopathy and macular degeneration, and various ischemic or vascular pathologies. A proteins' role in cell survival can also be suggested based on restricted expression in cells subjected to external stress such as oxidative damage, hypoxia, drugs such as cisplatinum, or irradiation. Metastases-associated genes can be implicated when expression is restricted to invading regions of a  
30 tumor, or is only seen in local or distant metastases compared to the primary tumor, or when a gene is upregulated during cell culture models of invasion, migration, or motility.



Chromosomal location can identify candidate targets for a tumor amplicon or a tumor-suppressor locus. Summaries of prevalent tumor amplicons are available in the literature, and can identify tumor types to experimentally be confirmed to contain amplified copies of a kinase gene which localizes to an adjacent region.

Based on these criteria several kinases immediately stand out as being of potential therapeutic relevance. The protein kinases can be divided into the following disease-relevant categories (nucleotide Seq ID #s in parentheses):

Tumor associated: Mok (SEQ ID NO:57), EPK2, AA316804 (SEQ ID NO:11), AA435956 (SEQ ID NO:48), AA278842 (SEQ ID NO:88), AA599286 (SEQ ID NO:89), AA826850 (SEQ ID NO:3), HRI (SEQ ID NO:73), MLK4 AA232253 (SEQ ID NO:82), AA883975 SGK 235 (SEQ ID NO:95), AA311714 (SEQ ID NO:101), MPSK1 (SEQ ID NO:110), R19609 (Seq ID111), AA383293 (SEQ ID NO:26).

Prostate-specific: AA234451 (SEQ ID NO:47), TSK4 (SEQ ID NO:93), RIP4 (SEQ ID NO:84), KIAA0965 (SEQ ID NO:8).

Oncogenic or proliferation associated: KIAA0781 (SEQ ID NO:38), AA789239 (SEQ ID NO:52), CCRK (SEQ ID NO:54), CLK4 (SEQ ID NO:55), H85389 (SEQ ID NO:97).

Neuronal restricted: CAMKKB (SEQ ID NO:66)

Hematopoietic expressed: PTK9L (SEQ ID NO:22), DRAK2 (SEQ ID NO:29), AI025291 (SEQ ID NO:94)

Angiogenic or endothelial expressed: DRAK1 (SEQ ID NO:31), MAK-V (SEQ ID NO:40), TRAD (SEQ ID NO:44), MOK (SEQ ID NO:57), AA08847 (SEQ ID NO:78), HGP\_66444466 (SEQ ID NO:79), RSK4 (SEQ ID NO:16).

Cell cycle regulated: AA454060 (SEQ ID NO:45), KIAA0999 (Mitotic – SEQ ID NO:32), AA579641 (Mitotic – SEQ ID NO:60), AA305176 (Mitotic – SEQ ID NO:6), AA018361 (S1 phase – SEQ ID NO:100).

#### VIII. Transgenic Animals.

A variety of methods are available for the production of transgenic animals associated with this invention. DNA can be injected into the pronucleus of a fertilized egg before fusion of the male and female pronuclei, or injected into the nucleus of an embryonic cell (*e.g.*, the nucleus of a two-cell embryo) following the initiation of cell division (Brinster *et al.*, Proc. Nat. Acad. Sci. USA 82: 4438-4442, 1985). Embryos can

be infected with viruses, especially retroviruses, modified to carry inorganic-ion receptor nucleotide sequences of the invention.

Pluripotent stem cells derived from the inner cell mass of the embryo and stabilized in culture can be manipulated in culture to incorporate nucleotide sequences of the invention. A transgenic animal can be produced from such cells through implantation into a blastocyst that is implanted into a foster mother and allowed to come to term. Animals suitable for transgenic experiments can be obtained from standard commercial sources such as Charles River (Wilmington, MA), Taconic (Germantown, NY), Harlan Sprague Dawley (Indianapolis, IN), etc.

The procedures for manipulation of the rodent embryo and for microinjection of DNA into the pronucleus of the zygote are well known to those of ordinary skill in the art (Hogan *et al.*, *supra*). Microinjection procedures for fish, amphibian eggs and birds are detailed in Houdebine and Chourrout (*Experientia* 47: 897-905, 1991). Other procedures for introduction of DNA into tissues of animals are described in U.S. Patent No., 4,945,050 (Sanford *et al.*, July 30, 1990).

By way of example only, to prepare a transgenic mouse, female mice are induced to superovulate. Females are placed with males, and the mated females are sacrificed by CO<sub>2</sub> asphyxiation or cervical dislocation and embryos are recovered from excised oviducts. Surrounding cumulus cells are removed. Pronuclear embryos are then washed and stored until the time of injection. Randomly cycling adult female mice are paired with vasectomized males. Recipient females are mated at the same time as donor females. Embryos then are transferred surgically. The procedure for generating transgenic rats is similar to that of mice (Hammer *et al.*, *Cell* 63:1099-1112, 1990).

Methods for the culturing of embryonic stem (ES) cells and the subsequent production of transgenic animals by the introduction of DNA into ES cells using methods such as electroporation, calcium phosphate/DNA precipitation and direct injection also are well known to those of ordinary skill in the art (Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, E.J. Robertson, ed., IRL Press, 1987).

In cases involving random gene integration, a clone containing the sequence(s) of the invention is co-transfected with a gene encoding resistance. Alternatively, the gene encoding neomycin resistance is physically linked to the sequence(s) of the invention.

Transfection and isolation of desired clones are carried out by any one of several methods well known to those of ordinary skill in the art (E.J. Robertson, *supra*)

DNA molecules introduced into ES cells can also be integrated into the chromosome through the process of homologous recombination (Capecchi, Science 244: 1288-1292, 1989). Methods for positive selection of the recombination event (*i.e.*, neo resistance) and dual positive-negative selection (*i.e.*, neo resistance and gancyclovir resistance) and the subsequent identification of the desired clones by PCR have been described by Capecchi, *supra* and Joyner *et al.* (Nature 338: 153-156, 1989), the teachings of which are incorporated herein in their entirety including any drawings. The final phase of the procedure is to inject targeted ES cells into blastocysts and to transfer the blastocysts into pseudopregnant females. The resulting chimeric animals are bred and the offspring are analyzed by Southern blotting to identify individuals that carry the transgene. Procedures for the production of non-rodent mammals and other animals have been discussed by others (Houdebine and Chourrout, *supra*; Pursel *et al.*, Science 244:1281-1288, 1989; and Simms *et al.*, Bio/Technology 6:179-183, 1988).

Thus, the invention provides transgenic, nonhuman mammals containing a transgene encoding a kinase of the invention or a gene effecting the expression of the kinase. Such transgenic nonhuman mammals are particularly useful as an *in vivo* test system for studying the effects of introduction of a kinase, or regulating the expression of a kinase (*i.e.*, through the introduction of additional genes, antisense nucleic acids, or ribozymes).

A "transgenic animal" is an animal having cells that contain DNA which has been artificially inserted into a cell, which DNA becomes part of the genome of the animal which develops from that cell. Preferred transgenic animals are primates, mice, rats, cows, pigs, horses, goats, sheep, dogs and cats. The transgenic DNA may encode human STE20-related kinases. Native expression in an animal may be reduced by providing an amount of anti-sense RNA or DNA effective to reduce expression of the receptor.

#### IX. Gene Therapy

Protein kinases of the invention, or their genetic sequences will also be useful in gene therapy (reviewed in Miller, Nature 357:455-460, 1992). Miller states that advances have resulted in practical approaches to human gene therapy that have demonstrated

positive initial results. The basic science of gene therapy is described in Mulligan (Science 260:926-931, 1993).

In one preferred embodiment, an expression vector containing protein kinase coding sequence is inserted into cells, the cells are grown *in vitro*, and then are infused in large numbers into patients. In another preferred embodiment, a DNA segment containing a promoter of choice (for example a strong promoter) is transferred into cells containing an endogenous gene encoding kinases of the invention in such a manner that the promoter segment enhances expression of the endogenous kinase gene (for example, the promoter segment is transferred to the cell such that it becomes directly linked to the endogenous kinase gene).

The gene therapy may involve the use of an adenovirus containing kinase cDNA targeted to a tumor, systemic kinase increase by implantation of engineered cells, injection with kinase-encoding virus, or injection of naked kinase DNA into appropriate tissues.

Target cell populations may be modified by introducing altered forms of one or more components of the protein complexes in order to modulate the activity of such complexes. For example, by reducing or inhibiting a complex component activity within target cells, an abnormal signal transduction event(s) leading to a condition may be decreased, inhibited, or reversed. Deletion or missense mutants of a component, that retain the ability to interact with other components of the protein complexes but cannot function in signal transduction may be used to inhibit an abnormal, deleterious signal transduction event.

Expression vectors derived from viruses such as retroviruses, vaccinia virus, adenovirus, adeno-associated virus, herpes viruses, several RNA viruses, or bovine papilloma virus, may be used for delivery of nucleotide sequences (*e.g.*, cDNA) encoding recombinant kinase of the invention protein into the targeted cell population (*e.g.*, tumor cells). Methods which are well known to those skilled in the art can be used to construct recombinant viral vectors containing coding sequences (Maniatis *et al.*, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, N.Y., 1989; Ausubel *et al.*, Current Protocols in Molecular Biology, Greene Publishing Associates and Wiley Interscience, N.Y., 1989). Alternatively, recombinant nucleic acid molecules encoding protein sequences can be used as naked DNA or in a reconstituted system *e.g.*, liposomes or other lipid systems for delivery to target cells (*e.g.*, Felgner *et al.*, Nature 337:387-8,

1989). Several other methods for the direct transfer of plasmid DNA into cells exist for use in human gene therapy and involve targeting the DNA to receptors on cells by complexing the plasmid DNA to proteins (Miller, *supra*).

In its simplest form, gene transfer can be performed by simply injecting minute amounts of DNA into the nucleus of a cell, through a process of microinjection (Capecchi, Cell 22:479-88, 1980). Once recombinant genes are introduced into a cell, they can be recognized by the cell's normal mechanisms for transcription and translation, and a gene product will be expressed. Other methods have also been attempted for introducing DNA into larger numbers of cells. These methods include: transfection, wherein DNA is precipitated with  $\text{CaPO}_4$  and taken into cells by pinocytosis (Chen *et al.*, Mol. Cell Biol. 7:2745-52, 1987); electroporation, wherein cells are exposed to large voltage pulses to introduce holes into the membrane (Chu *et al.*, Nucleic Acids Res. 15:1311-26, 1987); lipofection/liposome fusion, wherein DNA is packaged into lipophilic vesicles which fuse with a target cell (Felgner *et al.*, Proc. Natl. Acad. Sci. USA. 84:7413-7417, 1987); and particle bombardment using DNA bound to small projectiles (Yang *et al.*, Proc. Natl. Acad. Sci. 87:9568-9572, 1990). Another method for introducing DNA into cells is to couple the DNA to chemically modified proteins.

It has also been shown that adenovirus proteins are capable of destabilizing endosomes and enhancing the uptake of DNA into cells. The admixture of adenovirus to solutions containing DNA complexes, or the binding of DNA to polylysine covalently attached to adenovirus using protein crosslinking agents substantially improves the uptake and expression of the recombinant gene (Curiel *et al.*, Am. J. Respir. Cell. Mol. Biol., 6:247-52, 1992).

As used herein "gene transfer" means the process of introducing a foreign nucleic acid molecule into a cell. Gene transfer is commonly performed to enable the expression of a particular product encoded by the gene. The product may include a protein, polypeptide, anti-sense DNA or RNA, or enzymatically active RNA. Gene transfer can be performed in cultured cells or by direct administration into animals. Generally gene transfer involves the process of nucleic acid contact with a target cell by non-specific or receptor mediated interactions, uptake of nucleic acid into the cell through the membrane or by endocytosis, and release of nucleic acid into the cytoplasm from the plasma membrane or endosome. Expression may require, in addition, movement of the nucleic

acid into the nucleus of the cell and binding to appropriate nuclear factors for transcription.

As used herein "gene therapy" is a form of gene transfer and is included within the definition of gene transfer as used herein and specifically refers to gene transfer to express a therapeutic product from a cell *in vivo* or *in vitro*. Gene transfer can be performed *ex vivo* on cells which are then transplanted into a patient, or can be performed by direct administration of the nucleic acid or nucleic acid-protein complex into the patient.

In another preferred embodiment, a vector having nucleic acid sequences encoding a protein kinase polypeptide of the invention is provided in which the nucleic acid sequence is expressed only in specific tissue. Methods of achieving tissue-specific gene expression are set forth in International Publication No. WO 93/09236, filed November 3, 1992 and published May 13, 1993.

In all of the preceding vectors set forth above, a further aspect of the invention is that the nucleic acid sequence contained in the vector may include additions, deletions or modifications to some or all of the sequence of the nucleic acid, as defined above.

In another preferred embodiment, a method of gene replacement is set forth.

"Gene replacement" as used herein means supplying a nucleic acid sequence which is capable of being expressed *in vivo* in an animal and thereby providing or augmenting the function of an endogenous gene that is missing or defective in the animal.

#### X. Administration of Substances

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures, or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used, and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be formulated in animal models to achieve a circulating concentration range that initially

takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors, and major organs can be also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan, and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows: 1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition, and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, *Journal of American Veterinary Medical Assoc.*, 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness, or toxicity. Gross abnormalities in tissue are noted, and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5 Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

### EXAMPLES

The examples below are not limiting and are merely representative of various  
10 aspects and features of the present invention. The examples below demonstrate the isolation and characterization of the protein kinases of the invention.

#### EXAMPLE 1: Isolation of cDNA clones Encoding Novel Mammalian Protein Kinases Materials and Methods Identification from cDNA databases and isolation of clones encoding novel protein kinases

15

Novel kinases were identified from the public EST databases using a Hidden Markov model, abbreviated HMM (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. 1994. Hidden Markov models in computational biology: Applications to  
20 protein modeling. *J. Mol. Biol.*, 235:1501-1531). The model was built with 70 mammalian and yeast kinase catalytic domain sequences. These sequences were chosen from a comprehensive collection of kinases such that no two sequences had more than 50% sequence identity. ESTs were translated in six open reading frames and were searched against the model. ESTs that had a score of at least 10 against the HMM were  
25 then masked for repetitive sequences and vectors and were clustered using MSA. The resulting contigs were searched against known kinases to identify EST clones that encode novel kinases.

Approximately 40% of the ESTs encoding potentially novel kinases did not correspond to the correct EST upon sequence analysis. Most of these discrepancies were  
30 resolved by ordering additional clones, however, 14 remained unavailable. These 14 ESTs were amplified from a variety of single-stranded cDNA sources with primers derived from the corresponding EST entry as shown on Table 5. The PCR product was subcloned into a bluescript vector, digested to confirm the presence of a correct size insert and sequenced. Full sequencing of EST and PCR was carried out using a cycle sequencing Big-dye kit



with AmpliTaq DNA Polymerase, FS (ABI, Foster City, CA). Sequencing reaction products were run on an ABI Prism 377 DNA Sequencer.

Table 5: Primers used to clone PCR products corresponding to novel kinases

	ID#	ID#	Parent	5' primer	3' primer
sp	na	aa	Sequence	Sequence*	Sequence*
H	33	153	2R22-5-11	GAGATCGRNTTYAARGA RTTYGA	TGTCACNCCNAGNSWCCAN AYRTT
M	81	200	5R57_10_2_ m TESK2_m	GCTGCTGGACAGTGACT TGTATTT	GAAAGCAAAGCCTTCACAC CTT
H	67	187	5R69_17_2_h	CTCTCACCTCAGGAACT GG	GCTTGCGGATCTTCTCA
H	46	166	SGK309_h	GACATCCTGCCGGCCAA CTACG	CGGCCCTGGAGCTGCATCA CTA
M	67	228	5R72_16_2_h	TGCGCGACACCATTGAC CAG	CTCAGGGCTTACATACAGA G
H	45	165	5R72_8_2_h	AAAGGAGAACTACATT TGAAAAT	CTTCATCATCTCTAATACAT TGGTTGG
H	41	161	Z36720	CAAATTAAGATCATTGA CTTTGGG	GGAAACAAAGTCCTTGGCC TC
H	115	234	AL031652 - Pak6	GTGGACATCTGGTCCCT CG	GTAGGTCCTTCACTCTTGG AG

- degenerate oligonucleotide residue designation:

5 N= A,C,G or T

R= A or G

Y= C or T

S = C or G

W= A or T

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#### Full-length sequence extension of protein kinases using cDNA and genomic databases

Extension of partial cDNA sequences to encompass the full-length open-reading frame was carried out by iterative blastn searching of the cDNA databases listed in Table 6. All blastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1. The gapped blast algorithm is described in: (Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and

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PSI-BLAST: a new generation of protein database search programs". Nucleic Acids Res 25:3389-3402).

Table 6. Databases used for cDNA-based sequence extensions

Database	Database Date
LifeGold templates	Feb 2000
LifeGold compseqs	Feb 2000
LifeGold compseqs	Mar 2000
LifeGold compseqs	Apr 2000
LifeGold fl	Feb 2000
LifeGold flt	Apr 2000
NCBI human Ests	May 2000
NCBI murine Ests	May 2000
NCBI nonredundant	May 2000

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Extension of partial cDNA sequences to encompass the full-length open-reading frame was also carried out by iterative searches of genomic databases. Three methods were used. The first method made use of the Smith-Waterman algorithm to carry out protein-protein searches of the closest homologue or orthologue to the partial kinase. The target databases consisted of Genescan and open-reading frame (ORF) predictions of all human genomic sequence derived from the human genome project (HGP) as well as from Celera. The complete set of genomic databases searched is shown in Table 7 below. Genomic sequences encoding potential extensions were further assessed by blastp analysis against the NCBI nonredundant to confirm the novelty of the hit. The extending genomic sequences were incorporated into the cDNA sequence after removal of potential introns using the Seqman program from DNASTar. The default parameters used for Smith-Waterman searches were as shown next. Matrix: blosum 62; gap-opening penalty: 12; gap extension penalty: 2. Genescan predictions were made using the Genescan program as detailed in (Chris Burge and Sam Karlin "Prediction of Complete Gene Structures in Human Genomic DNA", JMB (1997) 268(1):78-94). ORF predictions from genomic DNA were made using a standard 6-frame translation.

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The second method for genomic sequence-based extensions made use of tBlastn searches of the homologue or orthologue to the partial kinase against the cDNA databases listed in Table 7. The recognition of significant hits in these databases made possible to identify bridging partial cDNA clones. The iterative application of the two methods made possible the assemblage of the virtual full-length sequence for a large number of the kinases presented in this application. All tblastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1.

The last method for defining cDNA extensions from genomic sequence used iterative searches of genomic databases through the Genescan program to predict exon splicing and the Genewise program (<http://www.sanger.ac.uk/Software/Wise2/>) to predict potential ORFs based on homology to the closest orthologue/homologue.

Table 7. Databases used for genomic-based sequence extensions

Database	Number of entries	Database Date
Celera v. 1-5	5,306,158	Jan 19/00
Celera v. 6-10	4,209,980	Mar 24/00
Celera v. 11-14	7,222,425	Apr 24/00
Celera v. 15	243,044	May 14/00
HGP all Genescan	25,885	Apr 04/00
HGP; Phase 0	4,944	May 04/00
HGP; Phase 1	28,478	May 05/00
HGP; Phase 2	1,508	May 04/00
HGP; Phase 3	9,971	May 05/00

#### Virtual Extensions

Human AA826850 (SEQ ID NO: 3, SEQ ID NO:124)

Blastn analysis of the partial AA826850 sequence revealed an extension to encompass the complete ORF in the Incyte EST 238299.1. A frame-shift correction at position 595 of this EST (marked by X in NA sequence) generated an uninterrupted ORF.

Human AA960957 (SEQ ID NO: 4, SEQ ID NO:125)

Since the initial filing of this application, the partial AA960957 sequence appeared in the public database as the full-length gene for a protein kinase encoded by a gene that maps adjacent to the *evc* (AJ250839) (ellis-van creveld syndrome and weyers acrodermal dysostosis) gene from 4p16.1.

5 Human 5R79-46-1\_h (SEQ ID NO: 5, SEQ ID NO:126)

Blastn analysis of the partial 5R79-46-1 sequence revealed an extension to encompass the complete ORF in the Incyte EST 463894.6. Since the initial filing of this application, the full-length virtual 5R79-46-1 appeared in the public database as the full-length gene for the TANK-binding kinase (TBK1) (Pomerantz, J.L. and Baltimore, D. (1999) EMBO J. 18 (23), 6694-6704). TBK1 participates in NF- $\kappa$ B activation through the formation of a signaling complex with TRAF2 and TANK.

Human AA305176 (SEQ ID NO: 6, SEQ ID NO:127)

Blastn analysis of the partial AA305176 sequence revealed an extension to encompass the complete ORF in the Incyte EST 220937.1.

15 Human AA256100 (SEQ ID NO: 8, SEQ ID NO:129)

Blastn analysis of the partial AA256100 sequence revealed an extension to encompass the complete ORF through the assembly of three partial clones: Incyte EST 480815.6, KIAA0965 (BAA76809) and AA256100.

Human AA210825 (SEQ ID NO: 9, SEQ ID NO: 130)

20 Blastn analysis of the partial AA210825 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte EST 014721.7, and the NCBI EST's AW01158 and AA210825. An insertion of two "N's" at positions 1915 and 1916 generated an uninterrupted ORF. Blastx analysis indicated the possibility of a start Met in the range of 400-450 nucleotides (i.e. compared to the closest homolog, human PKCmu (CAA53384.1). However, no Met was found in this region; rather ORF ends in an in-frame stop preceded by the sequence  
25 "RGLLAPGDPPCPPNPAPATPPSSRLPTLFSNFCDS". It is possible that part of the sequence covered by nucleotide positions 1-400 derived from AW01158 comes from an intron, explaining the absence of a start Met.

30 Human AA127299 (SEQ ID NO:10, SEQ ID NO:131)

No entries in the database extended this sequence. The 1684 bp insert of this EST contains a 1369 bp intron at the 3' end. Blastx and SW analysis of the 315 bp coding

region revealed homology to the extracatalytic C2 domain of PKC. This EST, may or may not encode a kinase.

Human AA316804 (SEQ ID NO:11, SEQ ID NO:132)

Since the initial filing of this application, the partial AA316804 sequence appeared in the public database as the full-length gene for the PKC family protein kinase EPK2 or PKCnu (AB015982).

Human H19102 (SEQ ID NO:14, SEQ ID NO:135)

Genewise and Genescan analyses of the partial H19102 sequence revealed an extension from the HGP phase 3 contig 3810672 to encompass the complete catalytic domain of this EST. Blastn analysis against the non-redundant database revealed that this gene is found in the cosmid AC005726 from chromosome 17. H19102 may encode a dual catalytic kinase given the homology to S6 kinase. Analysis of genomic sequence upstream of the 5' end of H19102 revealed a non-kinase gene oriented in the same polarity as H19102 suggestive of the start Met for H19102 being close to the 5' end of the H19102 sequence. From this analysis it is deduced that the second catalytic domain of H19102, if present, is most likely located within the 47334-185,215 bp region of the genomic sequence of AC005726.

Human AA476563 (SEQ ID NO:15, SEQ ID NO:136)

Since the initial filing of this application, the partial AA476563 sequence appeared in the public database as the full-length gene for the protein kinase RPS6KC1 (NM\_012424) (Zhang, H. et al Genomics (1999) 61, 314-318), which is an S6 kinase mapping to 12q12-q13.1.

Human AA626690 (SEQ ID NO:16, SEQ ID NO:137)

Since the initial filing of this application, the partial AA626690 sequence appeared in the public database as the full-length gene for the protein kinase RPS6KA6 (AF184965) (Yntema,H.G et al (1999) Genomics 62, 332-343), an S6 kinase commonly deleted in patients with complex X-linked (Xq21.1 ) mental retardation.

Human AI215680 (SEQ ID NO: 17, SEQ ID NO:138)

Since the initial filing of this application, the partial AI215680 sequence appeared in the public database as the full-length gene encoding a hypothetical protein (AAD30182) from the locus AC006530.4 from chromosome 14.

Human AA887783 (SEQ ID NO:21, SEQ ID NO:142)

Blastn analysis of the partial AA887783 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte 415390R6 and the NCBI EST's AA887783 and N94726. Since the initial filing of this application, the nearly full-length virtual AA887783 sequence appeared in the public database as the full-length gene encoding SGK3 (AF169035), a serum- and glucocorticoid-induced protein kinase (Kobayashi, T. et al (1999) Biochemical J. 344, 189-197.

Human R47805 (SEQ ID NO:22, SEQ ID NO:143)

A cDNA clone encoding the full-length ORF of R47805 was isolated using R47805 as a screening probe. A full-length form for R47805 has also appeared in the public database as

PTK9L (NM\_007284), an A6-related protein kinase.

Human H60215 (SEQ ID NO:23, SEQ ID NO:144)

Blastn analysis of the partial H60215 sequence revealed an extension to encompass the complete ORF in the public EST AI275726. This was confirmed through the full insert sequencing of this EST (2,310 bp) which corresponds to the sequence under SEQ ID NO:144.

A different stop codon was predicted for AI275726 compared to H60215 due to a single nucleotide insertion at position 1586 in AI275726. Evidence for the extra nucleotide comes from EST AI191922.

SGK324\_h orthologue of W30246\_m (SEQ ID NO:24, SEQ ID NO:145)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding to the human orthologue of murine W30246. Exons predicted from the following sequences were used for contig construction: Celera 17000189645083, 17000057549105 and 11000501939981; Incyte142404.1, HGP\_7249119, Incyte 7196489H1, Celera 11000501939981, 17000028165594; Incyte 7249119\_3. Celera 17000035772368, 11000502081575 and 17000140274329. The latter Celera sequence provides the N-terminus.

Human AA383293 (SEQ ID NO:26, SEQ ID NO:147)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding for AA383293. Exons predicted from the following sequences were used for contig construction: (numbers in parenthesis

refer to the aa sequence of the closest homolog (RU2S, NP\_057440) used for the Smith-Waterman query): N-term from Incyte 6010175\_2 (14-97), Incyte 6981981 (134-184) 7596749 (186-232) Celera 17000020789545 (243-301) CAB75619.1 (310-341)--(56-145 DCX homology) 6010175\_2, Celera 17000030058129 (241-262 DCX homology).

5 Human AA021445 (SEQ ID NO:32, SEQ ID NO:152)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. Contig reconstruction was as follows: nucleotides 1-802 from KIAA0999 (AB023216); nucleotides 803-4321 from full-insert sequence of AA021445. A pairwise alignment between the AA021445 and KIAA0999 revealed three  
10 inserts in the extracatalytic C-terminus of 48, 48 and 161 aminoacids. In addition, both AA021445 and KIAA0999 have 15 copies of a CAG repeat. Trinucleotide repeats are often found in genes that linked to neurodegenerative diseases.

Human 2R22-55-1 (SEQ ID NO:33, SEQ ID NO:153)

Blastn analysis revealed an extension in the Incyte EST clone 321074.1 to  
15 encompass the complete ORF corresponding to 2R22-55-1.

Human orthologue of AA544838\_m (SEQ ID NO:36, SEQ ID NO:156)

tBlastn analysis identified the partial human KIAA0135 (U79240) clone as the human orthologue of murine AA544838. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from  
20 Incyte406786.5, KFZp430051 and KIAA0135 (U79240).

Human orthologue of AI785735\_m (SEQ ID NO:38, SEQ ID NO:158)

tBlastn analysis identified the partial human KIAA0781 (AB018324) clone as the human orthologue of murine AI785735. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from Incyte  
25 986123.37 KIAA0781 (AB018324).

Human AA207220 (SEQ ID NO: 39, SEQ ID NO:159)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. The full ORF was reconstructed from Incyte 402740.1 and AA207220. Frame corrections: deletion of 441 and 595 over Inc402740.1 seq based on  
30 blastx to keep frame open; two n insertions 940, 941 over AA207220 to keep frame open.

Human AA426580 (SEQ ID NO:40, SEQ ID NO:160)

Since the initial filing of this application, the partial AA426580 sequence appeared in the public database as the full-length gene encoding MAK-V (AJ271722) from chromosome 21q22.1.

Human 5R79-54-1 (SEQ ID NO: 41, SEQ ID NO:161)

Genewise and Genescan analyses of the partial 5R79-54-1 sequence revealed an extension from genomic sequence to encode the full ORF for 5R79-54-1.

Human orthologue of AA542015\_m (SEQ ID NO: 42, SEQ ID NO:162)

tBlastn analysis identified KIAA1297 (AB037718). Blastn extended the KIAA1297 sequence to provide the C-terminus through the Incyte 224074.1 EST. The partial ORF consists of a dual catalytic domain flanked by 6 Ig domains and 2 fibronectin repeats. Based on homology to the bt drosophila protein (AAF59316.1), the human form of AA542015 is expected to be missing 16 Ig domains.

Human R19772 (SEQ ID NO:44, SEQ ID NO:164)

The full-length ORF for R19772 was isolated by screening a cDNA library using a probe derived from R19772. Since the initial filing of this application, the R19772 sequence appeared in the public database as the full-length gene encoding Trio (Duet) (AB011422). CDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 8. Isoforms for R19772

Kestrl Name	Kestrl AA Acc #	Isoform type	Source	Description*
Trad (Duet)	R19772	B	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762
		C	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762



				Deletion of 32 aa (160-191)
		D	Lung tumor	Deletion of Q at 616
				Deletion of 32 aa (160-191)
		E	Lung tumor	Deletion of Q at 616
				Deletion of 32 aa (160-191)

\* reference amino acid position are with respect to sequence of Trad (AB011422)

Human AA435956 (SEQ ID NO:48, SEQ ID NO:168)

5        Blastn analysis revealed an extension to encompass the nearly complete catalytic region of AA435956. 5' end sequence extension was provided by genomic locus AC007242.3\_h (range 44880-43801). Based on blastx analysis, the extended sequence encodes is full-length at the C-terminus.

Human AA397553 (SEQ ID NO: 51, SEQ ID NO:171)

10        Since the initial filing of this application, the partial AA397553 sequence appeared in the public database as the full-length gene encoding CRK7 (AF227198), a novel CDC2-related protein kinase that colocalizes with interchromatin granule clusters.

Human AA789239 (SEQ ID NO: 52, SEQ ID NO:172)

15        Since the initial filing of this application, the partial AA789239 sequence appeared in the public database as the full-length gene encoding NKIAMRE (AF130372), a novel kinase deleted in human leukemia.

Human AA631990 (SEQ ID NO:55, SEQ ID NO:175)

20        Blastn analysis revealed an extension to encompass the full-length ORF for AA631990. The full ORF was reconstructed from 253847.5 and AA631990 and AA207220. Frame corrections: delete 1 C at 1380, delete 2N's at 2033/2034.

Human AA557536 (SEQ ID NO:56, SEQ ID NO:176)

25        Blastn analysis revealed an extension to encompass full-length ORF for AA557536. The full ORF was reconstructed from AA557536, celera 11000504061899 and the Incyte 097089.1 EST. An 85bp intron was removed from AA557536.

Human N34132 (SEQ ID NO: 63, SEQ ID NO:183)

Full sequencing of EST N34132 (1.3 kb) confirmed that this cDNA encodes a novel NEK-subfamily kinase. Blast analysis against the EST database showed that four

EST sequences (AA283140, AA283140, AA282911 and N53011) extended the sequence of N34132 at the 3' end to form a 2.31 kb contig. Blast analysis of the new contig against the nonredundant public database showed that the N34132 extended contig overlapped (100% identity) over 228 bp at its 3' end with human KIAA0344 (AB002342), a 5,787 bp cDNA encoding a 1246 aa polypeptide. The 5' 790 bp of the KIAA0344 cDNA (encoding the 58 N-terminal protein sequence) were found to be divergent with respect to the extended 2.32 kb N34132 contig. Evidence that the extended N34132 contig (2.31kb) and KIAA0344 (AB002342) belong to the same gene is the following. First, blast analysis of the nucleotide sequences for N34132 and KIAA0344 against the NR database confirmed that these cDNA's are transcribed from the same genomic locus defined by two overlapping BACs (AC004765 and AC004803) from chromosome 12p13.3. Second, full sequence determination of a PCR fragment amplified from single-stranded cDNA confirmed the junction between the extended N34132 contig and KIAA0344\_h (AB002342). The 462 PCR product was amplified with primers CTCCTCAACAGACAGTGCAG (5' primer) and GACATTCTACTACTCGGTCTC (3' primer) designed from the N34132 extended contig and KIAA0344 sequences, respectively. The region of N34132 containing the start Met was isolated by PCR from a testis cDNA library (Clontech).

Human 5R69-17-2 (SEQ ID NO:67, SEQ ID NO:187)

The full-length ORF for 5R69-17-2 was isolated by screening a cDNA library using a probe derived from 5R69-17-2.

Human H85811 (SEQ ID NO:68, SEQ ID NO:188)

Tblastn, Smith-Waterman and blastn analyses using cDNA databases revealed an extension to encompass full-length ORF for H85811. The full ORF was reconstructed from Incyte ESTs 202971.8, 034583.3 and 034583.1 and public ESTs H85811 and AI570599.

Human R43524 (SEQ ID NO:73, SEQ ID NO:192)

Blastn analysis revealed an extension to encompass the complete catalytic region and the C-terminus of R43524. Since the initial filing of this application, the partial R43524 sequence appeared in the public database as the full-length gene encoding the heme-regulated initiation factor 2-alpha kinase (HRI) (AF181071).

Human AA088547 (SEQ ID NO:78, SEQ ID NO:197)

Genewise and Genescan analyses of genomic databases revealed an extension to encompass the complete ORF for AA088547.

Human orthologue of AA139478\_m (SEQ ID NO:80, SEQ ID NO:199)

Tblastn identified the Incyte 211475.1 as the potential full-length human orthologue of murine AA139478

Human AA232253 (SEQ ID NO:82, SEQ ID NO:201)

The full-length ORF for AA232253 was isolated by screening a cDNA library using a probe derived from AA232253. Since the initial filing of this application, the AA232253 sequence appeared in the public database as the full-length gene encoding SLK (AB011422). SLK is a stress-regulated mixed lineage kinase-like protein that activation of Rac and induction of apoptosis. cDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 9. Isoforms for AA232253

Kestrl Name	Kestrl AA Acc #	Isoform type	Description*
MLK4	AA232253	MLK4	Substitution of C for W at 346
		MLK4B	Different Cterm (332-800); seq in MLK4B is as shown in *

\* C-terminus specific to MLK4B

LPLAARMSEESYFESKTEESNSAEMSCQITATSNNGEGHGMNPSLQAMMLMGFGDI  
FSMNKAGAVMHSGMQINMQAKQNSS  
KTTSKRGRGKKVNMALGFSDFDLSEGDDDDDDDDGEEEDNDMDNSE

Human H97685 (SEQ ID NO:84, SEQ ID NO:203)

Blastn analysis revealed an extension to encompass the full-length ORF for H97685. The full ORF was reconstructed from Incyte 474824.1 and the public ESTs H97685 and M62021.

Human AI052250 (SEQ ID NO:87, SEQ ID NO:206)

Blastn analysis revealed an extension to encompass the full-length ORF for AI052250. The full ORF was reconstructed from Incyte 396868.1, the public partial cDNA FLJ10074 (minus intron) and the public ESTs and the public ESTs AI052250 and H97685, AI499220 and M62021.

5 Human AA278842 (SEQ ID NO:88, SEQ ID NO:206)

A nearly full-length cDNA (FL4F12) for AA278842 was isolated by screening a cDNA library using a probe derived from AA278842. A full-length virtual ORF was generated using FL4F12 and AA278842.

Human AA599286 (SEQ ID NO:89, SEQ ID NO:208)

10 Since the initial filing of this application, the partial AA599286 sequence appeared in the public database as a full-length ORF (AK000342).

Human AA425725 (SEQ ID NO:90, SEQ ID NO:209)

Since the initial filing of this application, the partial AA425725 sequence appeared in the public database as MSSK1, a serine kinase gene located from human chromosome Xq28.

15 Human SGK022 orthologue of AA060026\_m (SEQ ID NO:91, SEQ ID NO:210)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases revealed a potential human orthologue for murine AA060026. The full-length ORF for SGK022 was reconstructed from genomic locus AC022307.

20 Human AA399669 (SEQ ID NO:93, SEQ ID NO:212)

Blastn analysis revealed an extension to encompass the full-length ORF for AA399669. The full ORF was reconstructed as follows: sequence 1-1007 from AL136295.2; sequence 1008-2319 from AA399669 and Incyte 428177.1.

Human AA883975 (SEQ ID NO:95, SEQ ID NO:214)

25 Genescan and Genewise analyses of the genomic databases revealed an extension for AA883975 to encompass the full-length ORF

Human AA905446 (SEQ ID NO:96, SEQ ID NO:215)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases revealed an extension for AA905446 to encompass the full-length ORF. For the Smith-Waterman analysis murine STK22 (NP\_033462) was used as the closest orthologue. Contig formation: range 162133-163687 from HGP\_h 6921333\_9; removed intron (146-893) predicted from blastx analysis.

Human H29974 (SEQ ID NO: 97 SEQ ID NO:216)

Blastn analysis revealed an extension to encompass a complete catalytic ORF for AA399669. The nearly full-length ORF was reconstructed using Incyte 213829.1 and H29974.

5 Human AA215311 (SEQ ID NO:99, SEQ ID NO:218)

Blastn analysis revealed an extension to encompass the full-length ORF for AA21531. The full ORF was reconstructed from Incyte 067584.1, 022456.1, AA215311 and the reverse complement of CPG\_043208.

Human AA018361 (SEQ ID NO:100, SEQ ID NO:219)

10 The full-length ORF for AA018361 was isolated by screening a cDNA library using a probe derived from AA018361. This yielded clone Sug4-30. Clone Sug4-30, like multiple, independent cDNA clones contained a 181bp intron. The existence of intron-less RNA's was confirmed by a PCR reaction that generated a product that upon sequence analysis skipped the intron region. The full-length virtual ORF for AA018361 was  
15 generated through a contig between AL117482 (seq 1-367) and the sequence for clone Sug4-30.

Human orthologue of AA396601\_m (SEQ ID NO:106, SEQ ID NO:225)

tBlastn and Smith-Waterman analyses of genomic sequence revealed an extension to encompass the full catalytic region for the human orthologue of AA396601. The ORF  
20 was reconstructed from Incyte 018653.9 (7261449H1, 6891740J1) and genomic sequence CPG\_040010.

Human orthologue of AA671275\_m (SEQ ID NO:108, SEQ ID NO:227)

Since the initial filing of this application, a potential human orthologue for murine AA671275 appeared in the public database as the full-length ORF for vaccinia related  
25 kinase 3 (BAA90769).

Human H05721 (SEQ ID NO:111, SEQ ID NO:230)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for H05721.

Human AI086865 (SEQ ID NO:112, SEQ ID NO:231)

30 Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AI086865. The full-length ORF was reconstructed from Celera 17000102901516, Incyte 243269.1 and public AL1377531.

Human AA836348 (SEQ ID NO:113, SEQ ID NO:232)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AA836348.

Human R86668 (SEQ ID NO:14, SEQ ID NO:233)

5 The full-length ORF for R86668 was isolated by screening a cDNA library using a probe derived from R86668. Since the initial filing of this application, the R8668 sequence appeared in the public database as the full-length gene mitogen-activated protein kinase kinase kinase 6 (MAP3K6) (NM\_00467).

Human 2R41-9-4 (SEQ ID NO: 16, SEQ ID NO:235)

10 The full-length virtual ORF for 2R41-9-4 was generated using genomic sequence to provide the Nterminus for the partial ORF predicted from clone 2R41-9-4

Table 10. Sequences deleted from the provisional patent due to duplication with other genes in the patent

Prov. SEQ ID NO: (na)	Prov. SEQ ID NO: (aa)
160	196
213	214
215	216
122	126
119	123
148	184
4	20
7	23
205	206
14	30
15	31
35	56
42	63
51	72
44	65
77	91

78	92
79	93
80	94
157	193

## Results

Table 1 documents the results from the analysis of the nucleic acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family" and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. *et al.* (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "ORF Start", "ORF End", "ORF Length" refer to the open reading frame range and length as calculated by standard nucleic acid translation programs such as MapDraw (DNASar). "DNA Repeats" refers to regions of low complexity sequence or repetitive elements such as Alu, LINE, SINE, and LTR sequences. The chromosomal location (CHR localization) for 37 of the 110 novel protein kinases is shown on Table 1 (NA, not available). The methods for determining chromosomal position are outlined below, in Example 2.

Table 2 documents the results from the analysis of the amino acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family" and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. *et al.* (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "nraa Score", "ID match aa", "Identity", "Similar", "nraa Match Acc#", "Description" refer to the data obtained using a Smith-Waterman search of the amino acid sequence against the non-

redundant protein database (Matrix: Pam100; gap open/extension penalties 14/1). "Kinase Domain Start", "Kinase Domain End", "Profile Start" and "Profile End" refer to data obtained using a Hidden-Markov Model to define catalytic range boundaries. The profile has a length of 261 amino acids, corresponding to the complete protein kinase catalytic domain. Proteins in which the profile recognizes a full length catalytic domain have a "Profile Start" of 1 and a "Profile End" of 261. The boundaries of the catalytic domain within the overall protein are noted in the "Kinase Domain Start" and "Kinase Domain End" columns.

10 The following abbreviations were used for kinases:

ASK	Apoptosis signal-regulating kinase
CaMK	Ca <sup>2+</sup> /calmodulin-dependent protein kinase
CCRK	Cell cycle-related kinase
CDK	Cyclin-dependent kinase
CK	Casein kinase
DAPK	Death-associated protein kinase
DM	myotonic dystrophy kinase
Dyrk	dual-specificity-tyrosine phosphorylating-regulated kinase
GAK	Cyclin G-associated kinase
GRK	G-protein coupled receptor
GuC	Guanylate cyclase
HIPK	Homeodomain-interacting protein
IRAK	Interleukin-1 receptor-associated kin
MAPK	Mitogen activated protein kinase
MAST	Micotubule-associated STK
MLCK	Myosin-light chain kinase
MLK	Mixed lineage kinase
NIMA	NimA-related protein kinase
PKA	cAMP-dependent protein kinase
RSK	Ribosomal protein S6 kinase
RTK	Receptor tyrosine kinase



SGK	Serum and glucocorticoid-regulated kinase
STK	serine threonine kinase
ULK	UNC-51-like kinase

The following abbreviations were used for species

H	Human
M	Murine
R	Rat
FV	Fowlpox virus
MT	<i>M. thermoautotrophicum</i>
CE	<i>Caenorhabditis elegans</i>
DM	<i>Drosophila melanogaster</i>
OS	<i>Oryza sativa</i>
SP	<i>Schizosaccharomyces pombe</i>
TP	<i>Tetrahymena pyriformis</i>
PI	<i>Petunia inflata</i>
NC	<i>Neurospora crassa</i>
MSV	<i>Medicago sativa</i>
MSV	Moloney murine sarcoma virus
SA	<i>Squalus acanthias</i>
CS	<i>Cucumis sativus</i>
GM	<i>Glycine max</i>
LL	<i>Lilium longiflorum</i>
TV	<i>Trichomonas vaginalis</i>
MP	<i>Mycoplasma pneumoniae</i>
DD	<i>Dictyostelium discoideum</i>
SC	<i>Saccharomyces cerevisiae</i>
MT	<i>Methanobacterium thermoautotrophicum</i>

### Domain and Motif Identification

A Hidden Markov model (HMM) (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. (1994). Hidden Markov models in computational biology: Applications to protein modeling. J. Mol. Biol., 235:1501-1531) was used to identify, both catalytic and extracatalytic domains. Table 4 shows extra-catalytic domains that were identified using the HMM program. Other domains such as coiled-coil and pest motifs were identified as described next.

Potential coiled-coil domains were identified using the COILS program ([www.ch.embnet.org/software/COILS\\_form.html](http://www.ch.embnet.org/software/COILS_form.html)). The matrix used was MTIDK with windows of 14, 21, 28 amino acids. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region.

Protein sequences containing potential pest motifs were identified using the program PESTfind ([www.at.embnet.org/embnet/tools/bio/PESTfind/](http://www.at.embnet.org/embnet/tools/bio/PESTfind/)). PEST regions in proteins are by definition sequences that tend to be rich in proline, glutamic or aspartic acid, arginine and histidine; they have been associated with increased protein turnover rates (Rogers S. *et al.* (1986) Science 234, 364-368. The algorithm defines PEST sequences as hydrophilic stretches of amino acids greater than or equal to 12 residues in length. Such regions contain at least one P, one E or D and one S or T. They are flanked by lysine (K), arginine (R) or histidine (H) residues, but positively charged residues are disallowed within the PEST sequence. PESTfind produces a score ranging from about -50 to +50. By definition, a score above zero denotes a possible PEST region; a value greater than +5 defines a high probability that there is a PEST domain.

### **Identification of potential coiled-coil domains and PEST domains in N34132**

Potential coiled-coil domains were identified in N34132 (SEQ ID NO:183) using the COILS program. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region. The amino acid positions within N34231 scoring for potential coil-coil regions are shown below.

Table 11 coiled-coil domains predicted for N34132

Coiled-coil Region	Amino acid range	Length (aa)
1	124-147	24
2	437-451	15
3	495-526	32
4	1,723-1,749	27

Potential PEST domains were identified in N34132 using PESTfind, a value greater than +5 defines a high probability that there is a PEST domain. The amino acid positions within N34132 scoring for potential PEST regions are shown below.

Table 12 Potential Pest domains identified in N34132

PEST Region	Score	Amino acid range	Amino Acid Length
1	+ 4.91	54-95	42
2	+11.4	537-570	34
3	+31.08	1293-1304	12
4	+10.15	1543-1565	23
5	+ 6.17	1698-1732	35

## EXAMPLE 2. Chromosomal Localization of Novel Mammalian Protein Kinases

### Materials and Methods

Several sources were used to find information about the chromosomal localization of each of the genes described in this patent. First, the accession number for the nucleic acid sequence was used to query the Unigene database. The site containing the Unigene search engine is: <http://www.ncbi.nlm.nih.gov/UniGene/Hs.Home.html>. Information on map position within the Unigene database is imported from several sources, including the Online Mendelian Inheritance in Man (OMIM, <http://www.ncbi.nlm.nih.gov/Omim/searchomim.html>), The Genome Database (<http://gdb.infobiogen.fr/gdb/simpleSearch.html>), and the Whitehead Institute human physical map ([http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts\\_info?database=release](http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts_info?database=release)). For example, searching Unigene with W56561, an EST for a MAK-like kinase, the

following information is retrieved: Chr.14, D14S65-qTEL. The location of this gene on an "ideogram" of the cytogenetic map of chromosome 14 is also provided, showing that W56561 maps to the bottom of chromosome 14, between 14q31 and 14qTel. If Unigene has not mapped the EST, then the nucleic acid for the gene of interest is used as a query against databases, such as dbsts and htgs (described at [http://www.ncbi.nlm.nih.gov/BLAST/blast\\_databases.html](http://www.ncbi.nlm.nih.gov/BLAST/blast_databases.html)) containing sequences that have been mapped already. The nucleic acid sequence is searched using BLAST-2 at NCBI (<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast>) and is used to query either dbsts or htgs. In addition to the Whitehead and GDB sites mentioned above, Stanford University maintains a useful site for chromosomal mapping from STS data (<http://www-shgc.stanford.edu/RH/rhserverformnew.html>). Matches in htgs are often resolved immediately because the genomic region hit is annotated in the htgs entry. If an exact match match is found (defined roughly as 99% identity over a region of about 100 base pairs or longer, excluding any repetitive sequence), then the mapped position of the entry in the database is assigned to the original kinase query. Once a cytogenetic region has been identified by one of these approaches, disease association is established by searching OMIM (see above for URL) with the cytogenetic location. OMIM maintains a searchable catalog of cytogenetic map locations organized by disease. A thorough search of available literature for the cytogenetic region is also made using Medline (<http://www.ncbi.nlm.nih.gov/PubMed/medline.html>). References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, *et al.*, Am J Pathol, 1998, 152:1107-1123.

### Results

The chromosomal location for 37 of the 110 novel protein kinases is shown on Table 1. Three of the novel protein kinases were mapped to regions associated with cancer amplicons, as shown on this table. The regions were also cross-checked with the Mendelian Inheritance in Man database, which tracks genetic information for many human diseases, including cancer. References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, *et al.*, Am J Pathol, 1998, 152:1107-1123. Association of these mapped regions with other diseases is

documented in the Online Mendelian Inheritance in Man (OMIM)  
(<http://www.ncbi.nlm.nih.gov/htbin-post/Omim>).

### EXAMPLE 3: Generation of Specific Immunoreagents

#### 5 Materials and Methods

Peptide sequences to extra-catalytic regions of novel kinases are chosen which are not homologous to other known kinases based on a Smith Waterman homology search against the non-redundant protein database and predicted to be antigenic based on the DNASTar Protean program. These peptides are conjugated to KLH using Glutaraldehyde.

10 Rabbits are immunized with the KLH-peptide conjugates by four injections three weeks apart. The rabbits are bled ten and fourteen days following the third injection and bled out ten days after the fourth. The serum is checked against the peptide by ELISA.

Table 13. Peptides to be used as immunogens for raising antibodies

Clone Name	SEQ ID NO (aa)	Peptide Sequence	Amino Location
AA8256850	124	KSRDNSRDSSQSEND	339-353
		TEKLKRSQDLPREPLP	372-386
		RGWRPYDIHS	223-232
5R79-46-1	126	FEGPRRNKEVMYK	224-236
		KDDYNETVHKKTE	451-463
		GTHPKDRNVEKLQ	541-553
		EVSKYQEYTNELQET	643-657
AA256100	129	IDDTSNFDDFPESDI	405-419
		TEPDYKSKDWVFL	427-439
		EEKKLRRSQHARKET	61-75
AA210825	130	SNKDTLRKRHYWRLD	507-521
		RHTTRKSSTTLRE	488-500
		FQNNTTNRYEKEIPL	528-542
		GKHRKTGRDVAVK	668-680
		FPTKQESQLRNE	687-698

AA316804	132	ESHVHQEPSKRIPS	239-252
		HTKRKSSTMVKEGW	409-422
		PSDLDERDEEAVK	375-388
		SPGQGKDHKDLSTSI	543-557
R47805	143	EPVGRWDQDYDRAVL	44-58
		KPKGPGGKRGHKRLI	325-339
		PTDVAQLPSRVPRDA	219-233
AA234451	167	DPFDWEKTGNDGSLT	293-307
		HPRPQEKDVWEE	374-385
		RENTDEVFPDEQLSD	340-354
		RSEITQPDRDIPLVR	427-441
AA460132	180	LKSYSTSSKKARPVL	222-236
		KKLDEVRLRGRKRSM	237-251
		ETEKTAQGLSNLAKT	131-145
N34132	183	SGRRRRPTKSKGSKS	1848-1862
		PGTAPSKPPLTKAPV	1474-1488
		VDSDTQPKAPGIDD	1365-1378
		AHSLDKTSHSSTTGL	1253-1267
5R69-17-2	187	GTTREKTDRVKST	178-190
		HSEAPELHGKIRSSN	138-152
		DETVTPPQFSIV	87-98
		QYDVKSEIYS	204-213
AA278842	206	TVDPEKSVRDQAFKA	515-529
		DSSTADRWDDEDWGS	637-651
		SVSEDPTQLEEVEKD	539-553
AA836348	232	NAPTKRPRSSTVTEA	323-337
		LDSEEDYYTPQKVDV	514-528
		GDKASYRQPKHVEKL	409-423

EXAMPLE 4. Expression analysis of Novel Mammalian Protein KinasesGENE EXPRESSION ANALYSIS

## Tissue Arrays

"cDNA libraries" derived from a variety of sources were immobilized onto nylon  
5 membranes and probed with <sup>32</sup>P-labeled cDNA fragments derived from the gene(s) of  
interest.

Total RNA or mRNA was used as template in a reverse transcription reaction to  
generate single-stranded cDNAs (ss cDNA) that were tagged with specific sequences at  
each end. An oligo dT primer containing a specific sequence (CDS:

10 AAGCAGTGGTAACAACGCAGAGTACT30VN (V=A,G,C N=A,G,C,T)) anneals at  
the polyA track at the 3' end of the mRNA and the reverse transcriptase (MMLV  
RnaseH-) transcribes the antisense strand until it reaches the end of the RNA strand when  
it adds additional C residues. If a primer (SMII:

AAGCAGTGGTAACAACGCAGAGTACGCGGG or ML2G:

15 AAGTGGCAACAGAGATAACGCGTACGCGGG) ending with 3 Gs is added, it anneals  
to the added Cs and the MMLV recognizes the rest of the primer sequence as template and  
continues transcription. As a result, the synthesized cDNAs contain specific sequence tags  
at both the 5' and the 3' end. When the 5' and the 3' ends are tagged with the same  
sequence (CDS and SMII) it is referred to as "symmetric." When the 5' end is tagged  
20 with a different sequence than the 3' end (CDS and ML2G) is referred to as "asymmetric"  
A double-stranded "cDNA library" is then generated by PCR amplification using the  
3'PCR and ML2 primers (3' PCR: AAGCAGTGGT<sup>1</sup>AACAACGCAGAGT and ML2:  
AAGTGGCAACAGAGATAACGCGT) that anneal to the added sequence tags.

The amplified "cDNA libraries" were manually arrayed onto nylon membranes  
25 with a 384 pin replicator. The DNA was denatured by alkali treatment, neutralized and  
cross-linked by UV light. The arrays were pre-hybridized with Express Hyb (Clontech)  
and hybridized with <sup>32</sup>P labeled probes generated by random hexamer priming of cDNA  
fragments corresponding to the genes of interest. After washing, the blots were exposed to  
phosphorimaging cassettes and the intensity of the signal was quantified. The amount of  
30 the DNA on the arrays was also quantified by treating non-denatured or denatured arrays  
with Syber Green I or Syber Green II respectively (1:100,000 in 50mM Tris, pH8.0) for 2  
minutes. After washing with 50mM Tris, pH8.0, the fluorescent emission was detected

with a phosphorimager (Molecular Dynamics) and quantified. The amount of the arrayed DNA was used to normalize the hybridization signal and the corrected values are tabulated in Table 3.

## 5 Results

The results of the microarray expression analysis of the protein kinases presented in this application is shown in Table 3. Data presentation from left to right is as follows: "Tissue": tissue type of the cDNA; "Tumor sym", indicates that the tissue is derived from a tumor, "sym" refers to the fact that the 5' and 3' primers used to make the sample are the same; "Normal Sym", indicates normal tissue was used to make the sample, with symmetric primers as described above; "Tumor 1o", indicates that primary tumor tissue was used to make the cDNA; "Tumor cells", indicates that these cDNA samples were made from cultured tumor cells; "Normal", indicates that these samples are derived from normal tissue or cell lines; "Endos", indicates that these samples are derived from endothelium-related tissue sources; "p53" refers to the status, mutant or wild-type, of the p53 gene in the source samples. Normalized expression values are presented for each gene referred to by its SEQ ID# on the subsequent columns. Genes represented in expression Table 3 are: SEQ ID NO:3 (AA826850), SEQ ID NO:5 (TBK1), SEQ ID NO:6 (AA305176), SEQ ID NO:8 (AA256100), SEQ ID NO:9 (CAB43292), SEQ ID NO:11 (EPK2), SEQ ID NO:12 (PKNbeta), SEQ ID NO:14 (H19102), SEQ ID NO:16 (RSK4), SEQ ID NO:17 (AAD30182), SEQ ID NO:20 (SGK2), SEQ ID NO:22 (PTK9L), SEQ ID NO:26 (AA383293), SEQ ID NO:29 (DRAK2), SEQ ID NO:31 (DRAK1), SEQ ID NO:032 (AA015726), SEQ ID NO:40 (MAK-V), SEQ ID NO:044 (TRAD), SEQ ID NO:044 (TRAD), SEQ ID NO:45 (AA454060), SEQ ID NO:47 (AA234451), SEQ ID NO:48 (AA436054), SEQ ID NO:49 (AA626859), SEQ ID NO:51 (KIAA0904), SEQ ID NO:52 (AA789239), SEQ ID NO:54 (CCRK), SEQ ID NO:55 (CLK4), SEQ ID NO:56 (AA557536), SEQ ID NO:57 (W56561), SEQ ID NO:60 (AA579641), SEQ ID NO:63 (NEK7), SEQ ID NO:66 (CAMKKB), SEQ ID NO:68 (HIPK2), SEQ ID NO:72 (R19609), SEQ ID NO:73 (HRI), SEQ ID NO:78 (AA088547), SEQ ID NO:79 (AA449542), SEQ ID NO:082a (MLK4), SEQ ID NO:82 (MLK4b), SEQ ID NO:84 (RIP4), SEQ ID NO:88 (AA278842), SEQ ID NO:89 (AA195964), SEQ ID NO:90 (MSSK1), SEQ ID NO:93 (TSK4), SEQ ID NO:94 (AI025291), SEQ ID NO:95



(AA948538), SEQ ID NO:96 (AA905446), SEQ ID NO:97 (H85389), SEQ ID NO:100 (AA018361), SEQ ID NO:101 (AA311714), SEQ ID NO:110 (AA452647), SEQ ID NO:111 (AA310219), SEQ ID NO:112 (AI086865), SEQ ID NO:114 (MEKK6), and SEQ ID NO:116 (SuRTK106).

5

EXAMPLE 5. Kinase assays for Erk, JNK1 and p38 MAP kinases

293T cells were transiently transfected with HA- p38 or co-transfected with Flag-tagged wt MLK4A, kinase-dead MLK4A, wild-type MLK4B or kinase-dead MLK4B using Lipofectamine 2000 (Lifetech). Cells were lysed 36 hr post-transfection. Cell lysates normalized to contain equivalent amounts of HA-p38 were immunoprecipitated with anti-HA antibody (Mab HA-11, Babco). Immunoprecipitates were split in two portions, one portion was Western-blotted with anti- HA antibody and the other with a phospho-specific p38 antibody (Promega) to detect activated levels of p38. Activation of Erk1 and Jnk1 was measured similarly. (This example applies to AA232253 (SEQ ID NO:82, SEQ ID NO:201).)

10

15

Results:

In transient assays wild-type MLK4A and MLK4B (but not kinase-inactive MLK4A(K45M) or MLK4B(K45M)) activate Erk, JNK1 and p38 MAP kinases.

20

EXAMPLE 6. RAC1 guanine-exchange factor assay

293T cells were transiently transfected with HA-Rac1 or co-transfected with Flag-tagged Duet C, Duet E, Dbl and HA-Tiam-1. Cells were lysed 36 hour post-transfection. Cell lysates normalized to contain equivalent amounts of Rac1 were affinity precipitated with immobilized GST-PBD (p21-binding domain of Pak3). Bound proteins were Western blotted and probed with anti-HA antibody to detect levels of activated Rac1. ((This example applies to R199772 (Trad/Duet)(SEQ ID NO:44, SEQ ID NO:164).)

25

Results:

Duet C and Duet E both act as guanine nucleotide exchange factors on Rac1.

### CONCLUSION

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The molecular complexes and the methods, procedures, treatments, molecules, specific compounds described herein are presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains.

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed.

In particular, although some formulations described herein have been identified by the excipients added to the formulations, the invention is meant to also cover the final formulation formed by the combination of these excipients. Specifically, the invention includes formulations in which one to all of the added excipients undergo a reaction during formulation and are no longer present in the final formulation, or are present in modified forms.

In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush

group. For example, if X is described as selected from the group consisting of bromine, chlorine, and iodine, claims for X being bromine and claims for X being bromine and chlorine are fully described.

Other embodiments are within the following claims.

What is claimed is:

CLAIMS

1. An isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ  
5 ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ  
ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ  
ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ  
ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ  
ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ  
10 ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ  
ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ  
ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ  
ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ  
ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ  
15 ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ  
ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ  
ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ  
ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ  
ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ  
20 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ  
ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ  
ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ  
ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ  
ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ  
25 ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ  
ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ  
ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ  
ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

2. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises a nucleotide sequence that:

(a) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID

5 NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID  
10 NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID  
15 NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID  
20 NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
25 NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) is the complement of the nucleotide sequence of (a),

30 (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide;

(d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;

(e) is the complement of the nucleotide sequence of (d);

(f) encodes a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, wherein said domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;

(g) is the complement of the nucleotide sequence of (f);

(h) encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID

NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID  
NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID  
NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID  
NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID  
5 NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID  
NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID  
NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID  
NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID  
NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID  
10 NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID  
NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID  
NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID  
NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID  
NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID  
15 NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID  
NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID  
NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID  
NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID  
NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID  
20 NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID  
NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID  
NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID  
NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not  
all, of the domains selected from the group consisting of an N-terminal domain, a catalytic  
25 domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure  
region, and a C-terminal tail; or

(i) is the complement of the nucleotide sequence of (h).

3. The nucleic acid molecule of claim 1, further comprising a vector or promoter effective to initiate transcription in a host cell.



4. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is isolated, enriched, or purified from a mammal.

5. The nucleic acid molecule of claim 4, wherein said mammal is a human.

6. A nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of  
5 SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

7. The probe of claim 6, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

8       A recombinant cell comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

9. The cell of claim 8, wherein said polypeptide is a fragment of a protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

10. An isolated, enriched, or purified kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

11. The polypeptide of claim 10, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

12. The polypeptide of claim 10, wherein said polypeptide comprises:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all of the domains selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID



NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

13. The kinase polypeptide of claim 10, wherein said polypeptide is isolated, purified, or enriched from a mammal.

14. The kinase polypeptide of claim 13, wherein said mammal is a human.

15. The kinase polypeptide of claim 10, wherein said polypeptide is a AA144574, AA116841, AA256100, AA305176, AA210825, AA316804, AA980090, N42050, AA476563, AA626690, AA960957, H19102, AA045601, AA107515, AA109508 or AA887783 polypeptide.

16. The kinase polypeptide of claim 10, wherein said polypeptide is a H60215, AA197883, AA297313, W30246, AA172300, AA383293, AA542015, H01248, N23936, W44160, 2R22-5-11, 5R72-18-1, AA021445, AA207220, AA426580, AA544838, W90839, 5R79-54-1, AA839940, R19772 or 5R72-8-2 polypeptide.

17. The kinase polypeptide of claim 10, wherein said polypeptide is a AA234451 polypeptide.

18. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R65-16-1, AA061797, AA065538, AA124976, AA397553, AA435956, AA575635, AA626859, AA789239, A1086865, H17727, H29974, AA557536 or N28606 polypeptide.

19. The kinase polypeptide of claim 10, wherein said polypeptide is a AA631990 or W08549 polypeptide.

20. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R72-16-2, R19927 or R43524 polypeptide.

21. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R57-10-2 polypeptide.

5 22. The kinase polypeptide of claim 10, wherein said polypeptide is a AA232253 polypeptide.

23. The kinase polypeptide of claim 10, wherein said polypeptide is a AA430250, AA836348, R86668 or N34132 polypeptide.

10 24. The kinase polypeptide of claim 10, wherein said polypeptide is a AA098024 or SuRTK106 polypeptide.

25. The kinase polypeptide of claim 10, wherein said polypeptide is a R47805, AA099102, AA589241, H85811, AA013524, AA452647, AA840598, AA088547, AA139478, AA826850, R87679, W65887, H97685, W20810, AA599286, AA425725, AA103218, AA711829, AA060026, AA399669, AA758539, AA883975, AA948538, 15 AA018361, AA215311, AA311714, AA498104, 5R69-17-2, 5R69-23-3, 5R69-26-2, AA118352, AA396601, AA671275, AA278842, AA460132 or H05721 polypeptide.

26. An antibody or antibody fragment having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

27. The antibody or antibody fragment of claim 26, wherein said polypeptide comprises:

(a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ  
ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ  
ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ  
ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ  
ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ  
ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ  
ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ  
ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ  
ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ  
ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ  
ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ  
ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ  
ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ  
ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ  
ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ  
ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ  
ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ  
ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ  
ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ  
ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ  
ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and  
SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ  
ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ  
ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ  
ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ  
ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ  
ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ  
ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ  
ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ  
ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ  
ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID

NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID  
NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID  
NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID  
NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID  
5 NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID  
NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID  
NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID  
NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID  
NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID  
10 NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID  
NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID  
NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting  
of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a  
proline-rich region, a coiled-coil structure region, and a C-terminal tail.

28. A hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

29. A method for identifying a substance that modulates kinase activity comprising:

(a) contacting a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,

SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141,  
 SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146,  
 SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151,  
 SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156,  
 5 SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166,  
 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,  
 SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176,  
 SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181,  
 10 SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186,  
 SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191,  
 SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
 SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201,  
 SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206,  
 15 SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,  
 SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216,  
 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221,  
 SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,  
 SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231,  
 20 SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236,  
 SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241,  
 and SEQ ID NO:242 with a test substance;

(b) measuring the activity of said polypeptide; and

(c) determining whether said substance modulates the activity of said  
 25 polypeptide.

30. A method for identifying a substance that modulates kinase activity in a  
 cell comprising:

(a) expressing a kinase polypeptide in a cell, wherein said polypeptide  
 is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID  
 30 NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID  
 NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID  
 NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID



NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID  
NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID  
NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID  
5 NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID  
NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID  
NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID  
NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID  
NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID  
10 NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID  
NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID  
NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID  
NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID  
NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID  
15 NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID  
NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID  
NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID  
NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID  
NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID  
20 NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID  
NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

- (b) adding a test substance to said cell; and
- (c) monitoring a change in cell phenotype or the interaction between  
said polypeptide and a natural binding partner.

31. A method for treating a disease or disorder by administering to a patient in need of such treatment a substance that modulates the activity of a kinase selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

32. The method of claim 31, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

33. The method of claim 31, wherein said substance modulates kinase activity *in vitro*.

34. The method of claim 33, wherein said substance is a kinase inhibitor.

35. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:

- (a) contacting said sample with a nucleic acid probe which hybridizes  
5 under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide  
selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,  
SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129,  
SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134,  
SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,  
10 SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144,  
SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149,  
SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,  
SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164,  
15 SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169,  
SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179,  
SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184,  
SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
20 SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194,  
SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199,  
SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204,  
SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209,  
SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,  
25 SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219,  
SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,  
SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234,  
SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239,  
30 SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the  
nucleic acid sequence encoding said polypeptide, fragments thereof, or the complements  
of said sequences and fragments; and

(b) detecting the presence or amount of the probe:target region hybrid as an indication of said disease.

36. The method of claim 35, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

37. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:

(a) comparing a nucleic acid target region encoding said kinase polypeptide in a sample, wherein said kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ

ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding said kinase polypeptide, or one or more fragments thereof; and

- 5 (b) detecting differences in sequence or amount between said target region and said control target region, as an indication of said disease or disorder.

38. The method of claim 37, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

Table 1

Gene Name	SP	Proy Seq ID	NA	Proy Seq ID	AA	SEQ ID # na	SEQ ID # aa	Family	Group	Length NA	Length AA	ORF Start	ORF End	ORF Length	DNA Repeat	CHR Localization
N69117 h BARK2 h	H	1	1	1	1	122	122	AGC	GRK	2087	680	1	2084	2084	1	22q11
AA144574 m BARK2 m	M	1	1	1	1	123	123	AGC	GRK	1368	378	2	1135	1134	1	NA
AA826850 h	H	140	176	1	2	124	124	AGC	Mo3C11_Ca	1789	419	8	1264	1257	285.304	4p16.1
AA900957 h	H	11	27	1	3	125	125	AGC	Mo3C11_Ca	3274	414	65	1308	1242	1	10p11.2
SR19-06-1 h TBK1 h	H	207	208	1	5	126	126	AGC	Mo3C11_Ca	3013	728	93	2276	1987	1	10p11.2
AA305176 h	H	42	19.20	1	6	127	127	AGC	NDR	1421	320	53	1039	987	1	NA
AA116841 m	M	4.2	18.20	1	7	128	128	AGC	NDR	582	88	3	268	264	1	12p11
AA256100 h	H	1	19	1	6	129	129	AGC	NDR	4083	484	86	1477	1382	1	12p11
AA210805 h	H	5	21	1	6	130	130	AGC	PKC	3293	978	117	3050	2934	1	12p11 q13.3
AA127289 h	H	203	204	1	10	131	131	AGC	PKC	315	106	1	315	315	1	NA
AA316804 h ERK2	H	8	22	1	11	132	132	AGC	PKC	2613	890	1	2670	2670	1	2p21
AA2050 h PKR2	H	9	24	1	12	133	133	AGC	PKC	2670	889	1	2667	2667	1	NA
AA21071 m PKR2	M	5	24	1	13	134	134	AGC	PKC	979	205	2	616	615	1	NA
H19102 h	H	12	12	1	14	135	135	AGC	SGK	1155	384	1	1152	1152	1	CH17
AA476563 h RPS6KC1	H	10	25	1	15	136	136	AGC	SGK	1410	459	1	1407	1407	1	12p12 q13.1
AA286090 h RSK4	H	10	28	1	16	137	137	AGC	SGK	2238	745	1	2235	2235	1	12p12 q13.1
AA215680 h	H	227	228	1	17	138	138	AGC	SGK	1850	549	1	1847	1847	1	12p12 q13.1
SGK h	H	1	1	1	18	139	139	AGC	SGK	1758	431	1	1753	1753	1	12p12 q13.1
AA107515 m	M	1	1	1	19	140	140	AGC	SGK	2432	430	75	1304	1290	1	12p12 q13.1
AA109508 m	M	13	13	1	20	141	141	AGC	SGK	1348	244	2	733	732	1	NA
AA807783 h SGK3 SGK1	H	16	32	1	21	142	142	AGC	SGK	2250	448	36	1373	1338	1	NA
AA7805 h PTK9	H	131	107	1	22	143	143	AGC	SGK	1050	349	1	1047	1047	1	12p14.3
H60215 h	H	31	54	1	23	144	144	AGC	SGK	2310	440	470	1738	1320	1	12p14.3
SGK324 h	H	36	37	1	24	145	145	AGC	AMPK	3240	882	7	2082	2078	1	12p11.1 p13.3
W32240 m SGK324 m	M	36	37	1	25	146	146	AGC	AMPK	3240	882	7	2082	2078	1	12p11.1 p13.3
AA33293 h	H	36	59	1	26	147	147	AGC	AMPK	2424	688	1	2418	2418	1	NA
AA197883 m	M	34	55	1	28	148	148	AGC	AMPK	2424	688	1	2418	2418	1	NA
AA172300 h DRAX2	H	37	58	1	29	149	149	AGC	AMPK	2421	688	1	2418	2418	1	NA
AA172300 h DRAX2	H	37	58	1	30	150	150	AGC	AMPK	2421	688	1	2418	2418	1	NA
H01246 h DRAX1 h	H	40	61	1	31	151	151	AGC	AMPK	2421	688	1	2418	2418	1	NA
AA021445 h	H	45	66	1	32	152	152	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
7822.5.11 h	H	43	64	1	33	153	153	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
931237 h ACG33467	H	49	70	1	34	154	154	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
W98839 m	M	49	70	1	35	155	155	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA07865 h	H	48	66	1	36	156	156	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA544838 m 406786 m	M	48	66	1	37	157	157	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA765735 h	H	48	66	1	38	158	158	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA207220 h	H	48	67	1	39	159	159	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA426580 h MAK V h	H	47	68	1	40	160	160	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
338720 h	H	50	71	1	41	161	161	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
SGK088 h	H	39	68	1	42	162	162	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA542015 m SGK088 m	M	39	68	1	43	163	163	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
R19772 h	H	52	73	1	44	164	164	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
SR12.6.2 h	H	53	74	1	45	165	165	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
SGK300 h	H	159	165	1	46	166	166	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA234451 h	H	75	76	1	47	167	167	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA135946 h	H	82	96	1	48	168	168	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA626659 h	H	84	96	1	49	169	169	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA061797 m	M	81	95	1	50	170	170	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA307553 h CRK7	H	81	95	1	51	171	171	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA189239 h	H	85	98	1	52	172	172	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA124976 h	H	85	98	1	53	173	173	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA576035 m CCRK m	M	85	98	1	54	174	174	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA631980 h CLK4	H	105	107	1	55	175	175	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA557536 h	H	89	103	1	56	176	176	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	57	177	177	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	58	178	178	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	59	179	179	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	60	180	180	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	61	181	181	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	62	182	182	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	63	183	183	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	64	184	184	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	65	185	185	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	66	186	186	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	67	187	187	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	68	188	188	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	69	189	189	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	70	190	190	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	71	191	191	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	72	192	192	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	73	193	193	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	74	194	194	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	75	195	195	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	76	196	196	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	77	197	197	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	78	198	198	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	79	199	199	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	80	200	200	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	81	201	201	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	82	202	202	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	83	203	203	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	84	204	204	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	85	205	205	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H	90	104	1	86	206	206	AGC	AMPK	1245	414	1	1242	1242	1	12p11 q11
AA286090 h CLK4	H</															



Table 2

SP ID	Patent Seq ID	Family	Group	Protein	Length aa	ID match aa	% identity	% similar	Match ACC#	Description	Kinase Domain start	Kinase Domain end	Profile start	Profile end
H 1	122	AGC	GRK	2 7e-314	685	687	100	100	CAB4565.1	BAR2 [Homo sapiens]	191	453	1	261
M 2	123	AGC	GRK	1 30E-180	378	371	98	99	NP_037029.1	Adrenoreceptor kinase, beta 2 (G-protein-linked receptor kw)	3	143	121	261
H 3	124	AGC	GRK	5 80E-106	419	282	71	86	CAB7647.1	Serine/threonine protein kinase [Homo sapiens]	26	286	1	261
H 4	125	AGC	GRK	1 40E-137	414	414	100	100	CAB7647.1	Serine/threonine protein kinase [Homo sapiens]	23	283	1	261
H 5	126	AGC	GRK	0	729	729	100	100	NP_037386.1	TANK-binding kinase 1 [Homo sapiens]	9	304	1	261
H 6	127	AGC	NDR	1 20E-09	328	73	46	66	BAA76817.1	KIAA0973 protein [Homo sapiens]	35	310	1	261
M 7	128	AGC	NDR	1 30E-19	88	42	49	71	AAF55594.1	CG7719 gene product [Drosophila melanogaster]	24	44	242	261
H 8	129	AGC	NDR	6 10E-181	484	463	100	100	BAA76809.1	KIAA0965 protein [Homo sapiens]	90	363	1	261
H 9	130	AGC	PKC	8 80E-160	978	615	67	80	NP_002123.1	Protein kinase C, mu [Homo sapiens]	851	907	1	261
H 10	131	AGC	PKC	1 10E-10	105	42	42	57	P05127	Protein kinase C, beta-II type (PKC-BETA-2) [Homo sapiens]	19	24	256	261
H 11	132	AGC	PKC	0	890	890	100	100	NP_005404.1	Protein kinase C, nu [Homo sapiens]	578	832	1	261
H 12	133	AGC	PKC	9 4E-319	889	889	100	100	NP_037487.1	PKNbeta [Homo sapiens]	559	818	1	261
M 13	134	AGC	PKC	1 20E-108	205	204	100	100	JC7083	Protein kinase N beta [Homo sapiens]	1	134	126	261
H 14	135	AGC	S6K	3 60E-12	384	94	38	55	AAC82495.1	Ribosomal protein S6 kinase 3 [Homo sapiens]	81	333	1	261
H 15	136	AGC	S6K	2 80E-257	489	489	100	100	NP_036559.1	Ribosomal protein S6 kinase, 32KD, polypeptide 1 [Homo sapiens]	225	459	1	261
H 16	137	AGC	S6K	7 30E-178	745	745	100	100	NP_055311.1	Ribosomal protein S6 kinase, 90KD, polypeptide 6 [Homo sapiens]	330 & 683	428	1	261
H 17	138	AGC	S6K	9 80E-222	549	549	100	100	AAD30182.1	Unknown [Homo sapiens]	153	539	1	261
H 18	139	AGC	SGK	2 00E-103	431	430	100	100	NP_004109.1	SGK [Homo sapiens]	98	355	1	261
M 19	140	AGC	SGK	2 90E-157	430	426	99	99	NP_035491.1	Serum/glucocorticoid induced kinase [Mus musculus]	98	354	1	261
M 20	141	AGC	SGK	2 00E-76	244	244	100	100	AAF12757.2	Protein kinase [Homo sapiens]	1	168	24	261
H 21	142	AGC	SGK	4 10E-211	448	379	88	86	NP_270511.1	SGK-like protein SGK [Homo sapiens]	182	368	1	261
H 22	143	Atypical	AMPK	5 80E-216	349	349	100	100	NP_009215.1	Protein tyrosine kinase 9-like (A6-related protein) [Homo sapiens]	10	17	251	261
H 23	144	CAMK	AMPK	1 40E-19	440	88	39	61	CAA04119.1	Phosphoprotein [Homo sapiens]	40	333	1	261
H 24	145	CAMK	CAMK	1 50E-165	699	468	65	77	O15075	DCAMK1 [DOUBLECORTIN-LIKE AND CAM KINASE-LIKE 1]	388	625	1	261
M 25	146	CAMK	CAMK	1 60E-92	297	199	67	83	AAF28675.1	CPG16 [Mus musculus]	59	297	1	261
H 26	147	CAMK	CAMK	2 80E-48	708	181	44	60	O15075	DCAMK1 [DOUBLECORTIN-LIKE AND CAM KINASE-LIKE 1]	415	673	1	261
M 27	148	CAMK	CAMK	2 60E-31	808	147	55	73	AAF28675.1	CPG16 [Mus musculus]	514	771	1	261
M 28	149	CAMK	DAPK	3 10E-121	372	372	100	100	NP_004217.1	Death-associated protein kinase-related 2	33	293	1	261
M 30	150	CAMK	DAPK	7 90E-93	372	340	91	95	NP_004217.1	Death-associated protein kinase-related 2	32	293	1	261
H 31	151	CAMK	DAPK	1 20E-113	414	414	100	100	NP_004751.1	Death-associated protein kinase-related 1	61	321	1	261
H 32	152	CAMK	EMK	5 90E-185	1311	1053	80	80	BAA76843.1	Hypothetical protein F49C5.4 [Caenorhabditis elegans]	74	325	1	261
H 33	153	CAMK	EMK	1 20E-45	436	153	51	70	T22427	Hypothetical protein F49C5.4 [Caenorhabditis elegans]	74	325	1	261
H 34	154	CAMK	EMK	1 40E-32	438	122	48	65	AAC15093.1	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	56	307	1	261
M 35	155	CAMK	EMK	1 30E-184	728	729	100	100	AAC15093.1	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	59	340	1	261
H 36	156	CAMK	EMK	3 50E-126	462	462	100	100	AAC33487.1	R31237, partial CDS [Homo sapiens]	999	1256	1	261
M 37	157	CAMK	EMK	0	1330	1235	100	100	BAA09484.1	KIAA0135 gene is related to p1m-1 oncogene, [Homo sapiens]	1	158	23	261
M 38	158	CAMK	EMK	5 10E-59	230	183	79	85	BAA09484.1	KIAA0135 gene, related to p1m-1 oncogene, [Homo sapiens]	1	158	23	261
H 39	159	CAMK	EMK	3 00E-111	926	638	100	100	BAA34501.1	KIAA0781 protein [Homo sapiens]	20	271	1	261
H 40	160	CAMK	EMK	7 30E-80	829	367	57	69	NP_055655.1	KIAA0537 gene product [Homo sapiens]	53	304	1	261
H 41	161	CAMK	EMK	1 40E-244	714	714	100	100	NP_055401.1	Homomally upregulated neu tumor-associated kinase [Homo sapiens]	81	320	1	261
H 42	162	CAMK	MLCK	8 20E-76	874	211	83	80	AA73168.1	Skeletal muscle myosin light chain kinase [Gallus gallus]	570	825	1	261
M 43	163	CAMK	Tro	0	2286	2227	100	100	BAA92535.1	KIAA1297 protein [Homo sapiens]	820 & 1088	873 & 1356	1	261
M 44	164	CAMK	Tro	7 80E-37	127	67	99	99	BAA92535.1	KIAA1297 protein [Homo sapiens]	3	78	186	261
H 45	165	CAMK	Unque	0	1287	1284	100	100	NP_008995.1	STK with Dbl- and peckstin homology domains [Homo sapiens]	985	1239	1	261
M 46	166	CKI	CKI	5 00E-20	514	114	41	63	P25323	MLCK [Dictyostelium discoideum]	116	381	1	261
H 47	167	CKI	CKI	3 30E-49	508	181	53	65	AAF58340.1	CG11533 gene product [Drosophila melanogaster]	34	313	1	261
H 48	168	CKI	CKI	8 80E-98	478	188	57	68	AAF58340.1	CG11533 gene product [Drosophila melanogaster]	21	471	1	261
M 49	169	CKI	CDK	9 90E-39	266	138	62	79	NP_036527.1	PFTAIRE protein kinase 1 [Homo sapiens]	1	218	23	261
H 49	169	CKI	CDK	7 10E-46	247	148	59	75	NP_004187.1	Cyclin-dependent kinase-like 1 [CDC2-related kinase] [Homo sapiens]	1	181	23	261



Table 2 (cont'd)

M	50	170	CMGC	CDK	2.90E-64	296	193	65	78	NP_004187.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sapiens]	1	240	24	261
H	51	171	CMGC	CDK	1.10E-284	1490	1490	100	100	AAF38401.1	CDC2-related protein kinase 7 [Homo sapiens]	21	1020	1	261
M	52	172	CMGC	CDK	9.20E-101	534	377	82	82	AAF38509.1	NKIATRE [Homo sapiens]	4	385	1	261
M	53	173	CMGC	CDK	1.40E-128	337	225	79	96	AAF34871.1	NKIATRE alpha [Rattus norvegicus]	1	28	235	261
M	54	174	CMGC	CDK	3.00E-68	211	159	82	84	NP_038251.1	Cell cycle related kinase [Homo sapiens]	1	153	134	261
M	55	175	CMGC	CLK	1.50E-242	499	436	91	93	NP_031740.1	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sapiens]	177	493	1	261
H	56	176	CMGC	RCK	9.10E-89	544	343	57	64	AAO12719.1	Extracellular signal-regulated kinase 7, ERK7 [Rattus norvegicus]	13	305	1	261
H	57	177	CMGC	RCK	2.30E-189	419	419	100	100	NP_055041.1	Renal tumor antigen [Homo sapiens]	4	285	1	261
M	58	178	CMGC	RCK	1.50E-180	632	632	100	100	AAF37278.1	Intestinal cell kinase [Homo sapiens]	4	284	1	261
M	59	179	CMGC	RCK	1.60E-79	413	198	80	77	P20889	MECK [Rattus norvegicus]	109	364	1	261
H	60	180	Microbial PK	YGR262.sc	2.50E-45	253	102	46	67	AAF50799.1	CG10873 gene product [Drosophila melanogaster]	101	267	65	147
H	61	181	Other	C26C2.ce	2.30E-158	509	258	100	100	CAB70864.1	Hypothetical protein [Homo sapiens]	2	267	1	261
M	62	182	Other	C26C2.ce	1.80E-152	281	243	94	98	CAB70864.1	Hypothetical protein [Homo sapiens]	59	86	235	261
M	63	183	Other	C26C2.ce	6.70E-300	1852	1193	99	99	NP_055638.1	KIAA0344 gene product [Homo sapiens]	221	479	1	261
M	64	184	Other	C26C2.ce	1.10E-254	535	535	100	100	NP_037524.1	Nuclear receptor binding protein [Homo sapiens]	73	327	1	261
M	65	185	Other	C26C2.ce	2.50E-208	378	372	98	100	NP_037524.1	Nuclear receptor binding protein [Homo sapiens]	1	170	85	261
H	66	186	Other	CAMKK	3.80E-148	588	588	100	100	AAD31507.1	Ca2+/calmodulin-dependent protein kinase kinase beta [Homo sapiens]	165	448	1	261
H	67	187	Other	CTRI	9.90E-24	287	87	33	52	JQ1743	Hypothetical 33.6K protein - rabbit (Roroma virus)	24	285	1	261
H	68	188	Other	DYRK	0	1171	1137	97	99	AAD52586.1	Nuclear body associated kinase 1a [Mus musculus]	199	527	1	261
H	69	189	Other	DYRK	2.10E-280	553	553	100	100	NP_003573.1	Dual-specific tyrosine (Y)-phosphorylation regulated kinase 3	174	487	1	261
M	70	190	Other	DYRK	2.30E-95	168	149	80	96	NP_003573.1	Dual-specific tyrosine (Y)-phosphorylation regulated kinase 3	187	583	1	261
H	71	191	Other	E1FK	0	1649	1493	90	96	NP_038747.1	GCN2 eIF2alpha kinase [Mus musculus]	78	103	235	261
H	73	192	Other	E1FK	1.50E-220	630	630	100	100	NP_055228.1	Heme-regulated initiation factor 2-alpha kinase [Homo sapiens]	101	187	65	147
H	74	193	Other	Endop	2.50E-45	253	102	46	87	AAF50799.1	CG10873 gene product [Drosophila melanogaster]	116	150	116	147
M	75	194	Other	Endop	3.70E-45	216	100	45	84	AAF50799.1	CG10873 gene product [Drosophila melanogaster]	165	443	1	261
H	76	195	Other	IRAK	0	598	598	100	100	NP_009130.1	Interleukin-1 receptor-associated kinase M [Homo sapiens]	357	620	1	261
M	77	196	Other	IRAK	1.20E-170	392	293	75	85	NP_009130.1	Interleukin-1 receptor-associated kinase M [Homo sapiens]	516	777	19	261
H	78	197	Other	IRE	1.5e-323	922	746	82	89	NP_036146.1	Irf1, interferon-inducible protein 1 [Mus musculus]	32	318	1	261
H	79	198	Other	KYK2.dg	8.70E-40	225	102	45	50	AAF48758.1	CG8173 gene product [Drosophila melanogaster]	12	286	1	261
M	80	199	Other	KYK2.dg	5.90E-32	280	109	32	52	AAF48758.1	CG8173 gene product [Drosophila melanogaster]	12	286	1	261
M	81	200	Other	LIMK	2.80E-17	41	37	92	95	NP_009101.1	Lesli-specific kinase 2 [Homo sapiens]	18	259	101	128
M	82	201	Other	MLK	2.50E-282	800	789	100	100	AAF63490.1	Mixed lineage kinase [Homo sapiens]	16	259	1	261
H	83	202	Other	MLK	8.60E-251	835	835	100	100	AAD28632.1	Putative protein-tyrosine kinase [Homo sapiens]	483	723	1	261
H	84	203	Other	RIP	2.20E-158	634	385	100	100	BAA32317.1	KIAA0472 protein [Homo sapiens]	357	620	1	261
M	85	204	Other	RIP	5.30E-158	289	288	100	100	AAF03133.1	Receptor interacting protein 3 [Mus musculus]	7	27	181	202
H	86	205	Other	SCY1.sc	0	686	688	100	100	CAB55300.1	Hypothetical protein [Homo sapiens]	57	83	50	78
H	87	206	Other	SCY1.sc	1.70E-209	505	354	98	98	BAA92598.1	KIAA1360 protein [Homo sapiens]	32	327	1	261
H	88	207	Other	SCY1.sc	2.20E-157	808	396	45	61	AAF58933.1	CG1973 gene product [Drosophila melanogaster]	65	131	47	116
H	89	208	Other	SLOB?	7.40E-196	649	649	100	100	BAA91097.1	Unnamed protein product [Homo sapiens]	230	305	81	143
H	90	209	Other	SRPK	5.80E-252	533	533	100	100	NP_055185.1	Serine/threonine kinase 23 [Homo sapiens]	79	531	1	261
H	91	210	Other	STK22A	3.80E-53	268	122	48	70	NP_033461.1	Serine/threonine kinase 22A (spermogenesis associated) [Mus musculus]	10	265	1	261
M	92	211	Other	STK22	2.70E-52	268	127	48	68	NP_033461.1	Serine/threonine kinase 22B (spermogenesis associated)	10	265	1	261
H	93	212	Other	STK22A	4.80E-16	292	112	45	64	NP_033461.1	Serine/threonine kinase 22A (spermogenesis associated)	25	280	1	261
H	94	213	Other	STK22A	5.10E-123	358	322	90	98	NP_033461.1	Serine/threonine kinase 22B (spermogenesis associated) [Mus musculus]	12	272	1	261
H	95	214	Other	TSK	2.10E-33	273	122	46	62	NP_033461.1	Serine/threonine kinase 22A (spermogenesis associated)	12	267	1	261
H	96	215	Other	TSK	2.50E-32	216	93	41	58	NP_033461.1	Serine/threonine kinase 22B (spermogenesis associated)	1	213	7	261
H	97	216	Other	UNC	0.000062	333	57	36	56	AAD32787.1	Putative protein kinase [Arabidopsis thaliana]	1	329	1	261
M	98	217	Other	UNC	0.002492	412	53	37	52	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	80	408	1	261
H	99	218	Other	UNC	0.001096	341	50	36	56	BAA77341.1	UNC-51-like kinase (ULK) 2 [Mus musculus]	8	340	1	261
H	100	219	Other	UNC	1.80E-68	480	247	100	100	T17265	Hypothetical protein DKF2p34C131.1 - human (fragment)	57	313	1	261
H	101	220	Other	UNC	1.60E-208	565	468	98	96	BAA91270.1	Unnamed protein product [Homo sapiens]	4	265	1	261
H	102	221	Other	Uncue	6.70E-10	39	27	69	90	AAD00575.1	Serum-inducible kinase [Homo sapiens]	1	39	84	154

Table 2 (cont'd)

M	103	222	Other	Unque	0.00022	349	38	30	50	CAA18118.1	Serine/threonine protein kinase like protein [Arabidopsis thaliana]	80	159	1	88
H	104	223	Other	Unque	0.000126	704	54	30	45	BAA6578.1	KIAA1284 protein [Homo sapiens]	1	246	25	261
M	105	224	Other	Unque	0.007385	540	25	42	61	AAF47916.1	The gene product [Drosophila melanogaster]	9	104	168	261
M	106	225	Other	Unque	0.31334	540	52	30	42	P10162	SALIVARY PROLINE-RICH PROTEIN PO (ALLELE K) [Homo sapiens]	1	272	18	73
M	107	226	Other	Unque	0.022948	365	25	34	57	NP_006276.1	testis-specific kinase 1 [Homo sapiens]	68	96	42	71
M	108	227	Other	VRK	3.10E-263	474	474	100	100	BAA80769.1	Vaccinia related kinase 3 [Homo sapiens]	247	318	63	136
M	109	228	Other	VRK	1.20E-111	234	191	82	90	BAA80769.1	Vaccinia related kinase 3 [Homo sapiens]	7	78	63	136
H	110	229	Other	YPL236.sc	7.40E-144	305	304	100	100	AAC28337.1	MPSK [Homo sapiens]	20	290	1	261
H	111	230	Other	YQ09.ce	5.10E-49	581	135	43	63	AAF46188.1	CG4523 gene product [Drosophila melanogaster]	156	507	1	261
H	112	231	STE	NEK	3.30E-30	698	122	48	67	P51954	NEK1 (NIMA-RELATED PROTEIN KINASE 1) [Mus musculus]	4	251	1	261
H	113	232	STE	NEK	2.70E-119	838	357	86	86	AAD31939.1	(ACO07055) unknown [Homo sapiens]	52	306	1	261
H	114	233	STE	STE11	1.10E-291	1011	1011	100	100	NP_004663.1	mitogen-activated protein kinase kinase kinase 6 [Homo sapiens]	376	629	6	261
H	115	234	STE	STE20-02	7.70E-177	719	719	100	100	BAA84194.1	(AB040812) protein kinase PAK5 [Homo sapiens]	449	700	1	261
H	116	235	TK	RTK-20	4.90E-24	495	77	38	56	AAA08465.1	(U40827) protein tyrosine kinase [Mus musculus]	187	453	1	261
M	117	236	TK	RTK-20	5.30E-18	183	53	39	57	NP_032036.1	fibroblast growth factor receptor 3 [Mus musculus]	8	143	123	261
H	118	237	AGC	SGK	6.30E-112	367	367	100	100	AAF12757.2	SGK2alpha protein kinase [Homo sapiens]	35	292	1	261
H	120	238	CMGC	CDK	2.80E-137	452	452	100	100	NP_036251.1	Cell cycle related kinase [Homo sapiens]	4	287	1	261
H	121	239	Other	LMK	6.50E-233	555	555	100	100	NP_009101.1	Testis-specific kinase 2 [Homo sapiens]	62	293	5	261

164  
Table 3

[illegible]

[illegible]

DOCID <WO 0073469A2 1 >

[illegible]

167  
Table 3 (cont'd)[illegible]







170

USDOCID: AWC 0073469A2 1



[illegible]

Table 3 (cont'd)

[illegible]

[illegible]

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ADIRL1	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190	191	192	193	194	195	196	197	198	199	200	201	202	203	204	205	206	207	208	209	210	211	212	213	214	215	216	217	218	219	220	221	222	223	224	225	226	227	228	229	230	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	266	267	268	269	270	271	272	273	274	275	276	277	278	279	280	281	282	283	284	285	286	287	288	289	290	291	292	293	294	295	296	297	298	299	300	301	302	303	304	305	306	307	308	309	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329	330	331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348	349	350	351	352	353	354	355	356	357	358	359	360	361	362	363	364	365	366	367	368	369	370	371	372	373	374	375	376	377	378	379	380	381	382	383	384	385	386	387	388	389	390	391	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445	446	447	448	449	450	451	452	453	454	455	456	457	458	459	460	461	462	463	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565	566	567	568	569	570	571	57



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178

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Table 3 (cont'd)

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Table 3 (cont'd)[illegible]

[illegible]

182  
Table 3 (cont'd)[illegible]

Table 3 (continued)

Species	1960-69	1970-79	1980-89	1990-99	2000-09	2010-19	2020-29	2030-39	2040-49	2050-59	2060-69	2070-79	2080-89	2090-99	2100-109	2110-119	2120-129	2130-139	2140-149	2150-159	2160-169	2170-179	2180-189	2190-199	2200-209	2210-219	2220-229	2230-239	2240-249	2250-259	2260-269	2270-279	2280-289	2290-299	2300-309	2310-319	2320-329	2330-339	2340-349	2350-359	2360-369	2370-379	2380-389	2390-399	2400-409	2410-419	2420-429	2430-439	2440-449	2450-459	2460-469	2470-479	2480-489	2490-499	2500-509	2510-519	2520-529	2530-539	2540-549	2550-559	2560-569	2570-579	2580-589	2590-599	2600-609	2610-619	2620-629	2630-639	2640-649	2650-659	2660-669	2670-679	2680-689	2690-699	2700-709	2710-719	2720-729	2730-739	2740-749	2750-759	2760-769	2770-779	2780-789	2790-799	2800-809	2810-819	2820-829	2830-839	2840-849	2850-859	2860-869	2870-879	2880-889	2890-899	2900-909	2910-919	2920-929	2930-939	2940-949	2950-959	2960-969	2970-979	2980-989	2990-999	3000-1009	3010-1019	3020-1029	3030-1039	3040-1049	3050-1059	3060-1069	3070-1079	3080-1089	3090-1099	3100-1109	3110-1119	3120-1129	3130-1139	3140-1149	3150-1159	3160-1169	3170-1179	3180-1189	3190-1199	3200-1209	3210-1219	3220-1229	3230-1239	3240-1249	3250-1259	3260-1269	3270-1279	3280-1289	3290-1299	3300-1309	3310-1319	3320-1329	3330-1339	3340-1349	3350-1359	3360-1369	3370-1379	3380-1389	3390-1399	3400-1409	3410-1419	3420-1429	3430-1439	3440-1449	3450-1459	3460-1469	3470-1479	3480-1489	3490-1499	3500-1509	3510-1519	3520-1529	3530-1539	3540-1549	3550-1559	3560-1569	3570-1579	3580-1589	3590-1599	3600-1609	3610-1619	3620-1629	3630-1639	3640-1649	3650-1659	3660-1669	3670-1679	3680-1689	3690-1699	3700-1709	3710-1719	3720-1729	3730-1739	3740-1749	3750-1759	3760-1769	3770-1779	3780-1789	3790-1799	3800-1809	3810-1819	3820-1829	3830-1839	3840-1849	3850-1859	3860-1869	3870-1879	3880-1889	3890-1899	3900-1909	3910-1919	3920-1929	3930-1939	3940-1949	3950-1959	3960-1969	3970-1979	3980-1989	3990-1999	4000-2009	4010-2019	4020-2029	4030-2039	4040-2049	4050-2059	4060-2069	4070-2079	4080-2089	4090-2099	4100-2109	4110-2119	4120-2129	4130-2139	4140-2149	4150-2159	4160-2169	4170-2179	4180-2189	4190-2199	4200-2209	4210-2219	4220-2229	4230-2239	4240-2249	4250-2259	4260-2269	4270-2279	4280-2289	4290-2299	4300-2309	4310-2319	4320-2329	4330-2339	4340-2349	4350-2359	4360-2369	4370-2379	4380-2389	4390-2399	4400-2409	4410-2419	4420-2429	4430-2439	4440-2449	4450-2459	4460-2469	4470-2479	4480-2489	4490-2499	4500-2509	4510-2519	4520-2529	4530-2539	4540-2549	4550-2559	4560-2569	4570-2579	4580-2589	4590-2599	4600-2609	4610-2619	4620-2629	4630-2639	4640-2649	4650-2659	4660-2669	4670-2679	4680-2689	4690-2699	4700-2709	4710-2719	4720-2729	4730-2739	4740-2749	4750-2759	4760-2769	4770-2779	4780-2789	4790-2799	4800-2809	4810-2819	4820-2829	4830-2839	4840-2849	4850-2859	4860-2869	4870-2879	4880-2889	4890-2899	4900-2909	4910-2919	4920-2929	4930-2939	4940-2949	4950-295
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Table 3 (contd)

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Table 3 (cont'd)

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Table 3 (cont.)

[illegible]



Table 4

Gene Name	SPID#	na	ID#	aa	Family	Group	Length_AA	Extra-Catalytic Domains (Amino acid positions)
(69117_h beta_adren	H	1	122	AGC	GRK	GRK	688	Regulator of G protein signaling domain 54-175, PH domain 559-652
VA144574_m	M	2	123	AGC	GRK	GRK	378	PH domain 249-337
VA210825_h	H	9	130	AGC	PKC	PKC	978	Phorbol esters/diacylglycerol binding domain (C1 domain) 238-287, PH domain 497-577
VA316804_h	H	11	132	AGC	PKC	PKC	890	Phorbol esters/diacylglycerol binding domain (C1 domain) 155-204 and 272-321, PH domain 417-532
VA887783_h	H	21	142	AGC	SGK	SGK	446	PX domain 13-120
AA021445_h 3	H	32	152	CAMK	EMK	EMK	1311	Vitamin K-dependent carboxylation/gamma-carboxyglutamic (GLA) domain 1072-1113
R31237_1_h AAC3348	H	34	154	CAMK	EMK	EMK	729	UBA domain 327-365
106786_5_h	H	35	156	CAMK	EMK	EMK	1330	PAS domain 133-186, 247-280, 354-386
236720_h	H	41	161	CAMK	MLCK	MLCK	874	WD domain, G-beta repeat 674-711
SGK088_h	H	42	162	CAMK	Trio	Trio	2287	Immunoglobulin domain 1-62, 97-153, 221-277, 518-578, 1617-1678, Fibronectin type III domain 301-390, 1697-1779
R19772_h	H	44	164	CAMK	Trio	Trio	1287	RhoGEF domain 235-405; Fibronectin type III domain 870-955; Immunoglobulin domain 786-851, PH domain 19-528
17000139801197_h IRAH	H	76	195	Other	IRAK	IRAK	596	Death domain 26-106
AA088547_h	H	78	197	Other	IRE	IRE	922	PQQ enzyme repeat 39-76
AA232253_h	H	82	201	Other	MLK	MLK	800	SAM domain (Sterile alpha motif) 337-408
AA599286_h	H	89	208	Other	SLOB	SLOB	649	PX domain 16-122
AA836348_h	H	113	232	STE	NEK	NEK	836	Regulator of chromosome condensation (RCC1) 387-427, 427-480, 483-532, 598-650
PAK6_h	H	115	234	STE	STE20-02	STE20-02	719	P21-Rho-binding domain 11-69

## FIGURE 1A

SEQ ID NO: 122\_X69117\_H BARK2\_H  
MADLEAVLADVSYLMAMEKSKATPAARASKRIVLPEPSIRSVMQKYLAERNEITFDKIFN  
QKIGFLLFKDFCLNEINEAVPQVKFYEEIKEYEKLDNEEDRLCRSRQIYDAYIMKELLSC  
SHPFSKQAVEHVQSHLSKKQVTSTLFQPYIEEICESLRGDI FQKFMESDKFTRFCQWKNV  
ELNIHLTMNEFSVHRI IGRGGFGEVYGCRKADTGKMYAMKCLDKKRI KMKQGETLALNER  
IMLSLVSTGDCPFI VCMTYAFHTPDKLCFILDLMNGGDLHYHLSQHGVFSEKEMRFYATE  
IILGLEHVHNRFFVYRDLKPANILLDEHGHARISDLGLACDFSKKKPHASVGTHGYMAPE  
VLQKGTAYDSSADWFSLGCMFLKLLRGHSPFRQHKTCDKHEIDRMTLTVNVLPDFTFSPE  
LKSLLLEGLLQRDVSKRLGCHGGGSQEVKEHSFFKGVWDQHVYLVQKYPPLIPPRGEVNAA  
DAFDIGSFDEEDTKGIKLLDCDQELYKNFPLVISERWQQEVTETVYEAVNADTDKIEARK  
RAKNKQLGHEEDYALGKDCIMHGYMLKLGPNFLTQWQRRYFYLFNRLLEWRGEGESRQNL  
LTMEQILSVEETQIKDKKCILFRIKGGKQFVLQCESDPEFVQWKKELENETFKEAQRLLRR  
APKFLNKPRSGTVELPKPSLCHRNSNGL

SEQ ID NO: 123\_AA144574\_M BARK2\_M  
CFVVYRDLKPANILLDEYGHVRI SDLGLACDFSKKKPHASVGTHGYMAPEVLQKGTCTYDS  
SADWFSLGCMFLKLLRGHSPFRQHKTCDKHEIDRMTLTVNVQLPDFAFSPELRSLLLEGLLQ  
RDVSQRLGCGGGGARELKEHIFFKGIDWQHLYLRKYPPPLIPPRGEVNAA DAFDIGSFDE  
EDTKGIKLLDCDQDLYKNFPLVISERWQQEVTETIYDAVNADTDKIEARKKAKNKQLGQE  
EDYAMGKDCIMHGYMLKLGPNFLTQWQRRYFYLFNRLLEWRGEGESRQSLTMEQIMSVE  
ETQIKDRKCILLRIKGGKQFVLQCESDPEFAQWLKELTCTFNEAQRLLRRAPKFLNKPRA  
AILEFSKPPLCHRNSNGL

SEQ ID NO: 124\_AA826850\_H  
MGSSMSAATARRPVFDDKEDVNFDFHFI LRAIGKGSFGKVCIVQKRDTEKMYAMKYMKNQ  
QCIERDEVNRNVFRELEILQEIEHVFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVQ  
FSEDTVRLYICEMALALDYLRGQHI IHRDVKPDNILLDERGHAHLTDFNIATIIKDGERA  
TALAGTKPYMAPEIFXS FVNGGTGYSFEVDWWSVGVMAYELLRGWRPYDIHSSNAVESLV  
QLFSTVSVQYVPTWSKEMVALLRKLTVNPEHRLSSLQDVQAAPALAGVLWDHLSEKRVE  
PGFVPNKGRLLHCDPTFELEEMILESRLHKKKKRLAKNKS RDNSRDSSQSENDYLQDCLD  
AIQQDFVIFNREKLKRSQDLPREPLPAPESRDAAEPVEDEAERSALPMCGPICPSAGSG

SEQ ID NO: 125\_AA960957\_H  
MGGNHSHPVPVFDENEEVNFDFHFI LRAIGKGSFGKVCIVQKRDTEKMYAMKYMKNQKCI  
ERDEVNRNVFRELQIMQGLEHPFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVHFTE  
GTVKLYICELALALEYLQRYHI IHRDIKPDNILLDEHGHVHITDFNIATVVKGAERASSM  
AGTKPYMAPEVFQVYMDRGPYSPVDWWSLGITAYELLRGWRPYEIH SVTPIDEILNMF  
KVERVHYSSTWCKGMVALLRKLTKDPESRVSSLHDIQSVPYLADMNWDVAFKKALMPGF  
VPNKGRLLNCDPTFELEEMILESPLHKKKKRLAKNRSRDGT KDSCPLNGHLQHCLTVRE  
EFIIFNREKLRRQQGGSQLLDTSRGGGQAQSKLQDGCNNNLLTHTCTRGCS

SEQ ID NO: 126\_TBK1\_H  
MQSTSNHLWLLSDILGQATANVFRGRHKKTGDLFAIKVFNNISFLRPVDVQMREFEVLK  
KLNHKNIVKLF AIEETTTRHKVLIMEFCPCGSLYTVLEEPSNAYGLPESEFLIVLRDVV  
GGMNHLRENGIVHRDIKPGNIMRVIGEDGQSVYKLTDFGAARELEDDEQFVS LYGTEEYL  
HPDMYERAVLRKDHQKKYGATVDLWSIGVTIFYHAATGSLPFRPFEGPRRNKEVMYKIITG  
KPSGAISGVQKAENGPIDWSDMPVSCSLSRGLQVLLTPVLANILEADQEKCWGFDQFFA  
ETSDILHRMVIHVFSLQOMTAHKIYIHSYNTATIFHEL VYKQTKI ISSNQELIYEGRRLV  
LEPGRLAQHFPKTTEENPIFVVSREPLNTIGLIYEKISLPKVHPRYDL DGDASMAKAITG  
VVCYACRIASTLLLYQELMRKGIRWLI ELIKDDYNETVHKKTEVVITLDFCIRNIEKTVK

## FIGURE 1B

VYEKLMKINLEAAELGEISDIHTKLLRLSSSQGTIETSLQDIDSRLSPGGSLADAWAHQE  
GTHPKDRNVEKLVLLNCMTEIYYQFKKDKAERRLAYNEEQIHKFDKQKLYYHATKAMTH  
FTDECVKKYEAFLNKSEEWIRKMLHLRKQLLSLTNQCDFIEEEVSKYQEYTNELQETLFC  
KMFTASSGIKHTMTPIYPSSNTLVEMTLGMKKLKEEMEGVVKELAENNHILERFGSLTMD  
GGLRNVDC

SEQ ID NO: 127\_AA305176\_H

MDPTAGSKKEPGGGAATEEGVNRIVAPKPPSIEEFSIVKPISRGAFGKVYLQKGGKLYA  
VKVVKKADMINKNMTHQVQAERDALALSKSPFIVHLYYSLQSANNVYLVMEYLIGGDVKS  
LLHIYGYFDEEMAVKYISEVALALDYLHRHGIHRDLKPDNMLISNEGHIKLTDFGLSKV  
TLNRDINMMDILTPSPMAKPRQDYSRTPGQVLSLISLGFNTPIAEKNQDPANILSACLS  
ETSQLSQGLVCPMSVDQKDTTPYSSKLLKSCLETVASNPGMPVKCLTSNLLQSRKRLATS  
SASSQSHTFISSVESECHSSPKWEKDCQV

SEQ ID NO: 128\_AA116841\_M

TRPIPWPEGEEKLSDNAQSAMDMLLTIDDSKRAGMRELKQHPLFSEVDWENLQHQTMPFV  
PQPDDETDSYFEARNNAQHLLTVSGFSL

SEQ ID NO: 129\_AA256100\_H

MAMTAGTTTTFPMSNHTRERVTVAKLTLENFYSNLILQHEERETRQKKLEVAMEEEGLAD  
EEKKLRRSQHARKETEFRLRLKRTRLGLDDFESLKVIGRGAFGEVRLVQKKDTGHIYAMKI  
LRKSDMLEKEQVAHIRAERDILVEADGAWVVKMFYSFQDKRNLYLIMEFLPGGDMMTLLM  
KKDTLTEEETQFYISETVLAIDAIHQLGFIHRDIKPDNLLDAGHVKLSDFGLCTGLKK  
AHRTEFYRNLTNPPSDFSQNMNSKRKAETWKKNRRQLAYSTVGTDPDYIAPEVFMQTGY  
NKLCDWWSLGVIMYEMLIGYPPFCSETPQETYRKVMNWKETLVFPPEVPISEKAKDLILR  
FCIDSENRI GNSGV EIKGHPFFEGVDWEHIRERPAAPIEIKSIDDTSNFDDFPESDIL  
QPVPNTTEPDYKSKDWVFLNYTYKRFEGLTQRGSIPTYMKAGKL

SEQ ID NO: 130\_AA210825\_H

DSLLPTPALGTPLPWPVVGSLRTPLSLESTRSPTQRLLPSTPKDPAILRSPPPARSFLG  
SPLSHHLLTRSRGSRTQGPPGPPGGSRVGSRRAVPGLPWP PPPHY PAGLPGPSPGGPSPP  
PPGGLELQSPPLLPQIPAPGSGVSFHIQIGLTREFVLLPAASELAHVQKLACSIVDQKF  
PECGFYGLYDKILLFKHDPTSANLLQLVRSSGDIQEGDLVEVVLASATFEDFQIRPHAL  
TVHSYRAPAFCDHCGEMLFGLVRQGLKCDGCGLNHYHKRCAFSIPNNCSGARKRRLSSTSL  
ASGHSVRLGTSES LPCTAEELSRSTTELLPRRPPSSSSSSSASSYTGRPIELDKMLLSKV  
KVPHTFLIHSYTRPTVCQACKLLKGLFRQGLQCKDCKFNCHKRCATRPNDCLGEALIN  
GDVPMEEATDFSEADKSALMDESEDSGVI PGSHSENALHASEEEEEEGEGGKAQSSSLGYIPL  
MRVVQSVRHTTRKSSTTLREGWVVHYSNKDTLRKRHYWRLDCKCITL FQNNTTNRYEKEI  
PLSEILTVEAQNFSLVPPGTNPCHCFEIVTANATYFVGEMPGGT PGGPSGQGAEAARGLX  
ETAIRQALMPVILQDAPSAPGHAPHRQASLSISVSNSQIQENVDIATVYQIFPDEVLGSG  
QFGVVYGGKHKRKTGRDVAVKVIDKLRFP TKQESQLRNEVAILQSLRHPGIVNLECMFETP  
EKVFVVMKHLHGDMLLEMILSSEKGR LPERLTFLITQILVALRHLHFKNIVHCDLKPENV  
LLASADFPQVKLCDFGFARIIGEKSFRRSVGTPAYLAPEVLLNQGYNRSLDMWSVGVI  
MYVSLSGTFPFNEDEDINDQIQNAAFMYPASPSHISAGAILINNLLQVKMRKRYSDVK  
SLSHPW LQEYQTWLDLRELEGKMGERYITHESDDARWEQFAAEHPLPGSGLP TDRDLGGA  
CPPQDHDMQGLAERISVL

SEQ ID NO: 131\_AA127299\_H

IQFIIVGAKDLLAMDSNGLSDPYIKITNLSQKTKVIKKTLTPTWNETFFVHFPEKTTLEI  
ECWDHDTFSDDFIGKASISLAEIPALAEVDMWIDMKTKKGEFAGK



## FIGURE 1C

SEQ ID NO: 132\_AA316804\_H

MSANNSPPSAQKSVLPTAIPAVLPAASPCSSPKTGLSARLSNGSFSAPSALTNSRGSVHTV  
SFLQLIGLTRESVTIEAQELSLSAVKDLVCSIVYQKFPECGFFGMYDKILLFRHDMNSEN  
ILQLITSADEIHEGDLVEVVLALATVEDFQIRPHTLYVHSYKAPTFCDYCGEMLWGLVR  
QGLKCEGCGLNYHKRCAFKIPNNCSGVRKRRLSNVSLPGPGLSVPRFLQPEYVALPSEES  
HVHQEPSKRIPSWSGRPIWMEKMVMCRVKVPHTFAVHSYTRPTICQYCKRLLKGLFRQGM  
QCKDCKFNCHKRCASKVPRDCLGEVTFNGEPSSLGTDTDIPMDIDNNDINSRSSRGLDDT  
EESPSPEDKMFFLDPSDLDVERDEEAVKTI SPSTSNNIPLMRVVQSIKHTKRKSSTMVKE  
GWMVHYTSRDNLKRHYWRDLDSKCLTLFQNESGSKYYKEIPLSEILRISSPRDFTNISQG  
SNPHCFEII TDTMVYFVGENNGDSSHPVLAATGVGLDVAQSWEKAIRQALMPVTPQASV  
CTSPGQGDHKLSTSI SVSNCQIQENVDISTVYQIFADEVLGSGQFGIVYGGKHKRKTGR  
DVAIKVIDKMRFPPTKQESQLRNEVAILQNLHHPGIVNLECMFETPERVFVMEKLHGDML  
EMILSSEKSRPERITKFMVTQILVALRNLHFKNIVHCDLKPENVLLASAEFPQVKLCD  
FGFARIIGEKSFRRSVVGTPAYLAPEVLRSKGYNRSLDMWSVGVIIYVSLSGTFPFNEDE  
DINDQIQNAAFMYPPNPWREISGEAIDLINLLQVKMRKRYSDKSLSHPLWLDYQOTWLD  
LREFETRIGERYITHESDDARWEIHAYTHNLVYPKHFIMAPNPDDMEEDP

SEQ ID NO: 133\_PKNBETA\_H

MEEGAPRQPGPSQWPPPEDEKEVIRRAIQKELKIKEGVENLRRVATDRRHLGHVQQLLRSS  
NRRLEQLHGELRELHARILLPGPGPGAEPVASGPRPWAEQLRARHLEALRRQLHVELKV  
KQGAENMTHTCASGTPKERKLLAAQQLRDSQLKVALLRMKISSLEASGSPEPGPELLA  
EELQHRHLHVEAAVAEGAKNVVKLLSSRRTQDRKALAEQAQLQESSQKDLLRLALEQLL  
EQLPPAHPLRSRVTRELRAAVPGYPQPSGTPVKPTALTGTLOVRLLGCEQLLTAVPGRSP  
AAALASSPSEGWLRTKAKHQGRGELASEVLAVLKVDNRVVGQTGWGQVAEQSWDQTFVI  
PLERARELEIGVHWRDWRQLCGVAFLRLEDFLDNACHQLSLSLVPQGLLFAQVTFCDPVI  
ERRPRLQRQERIFSKRRGQDFLRRSQMNLGMAAWGRLVMNLLPPCSPSTISPPKGCPR  
PTTLREASDPATPSNFLPKKTPLGEEMTPPKPPRLYLPOEPTSEETPRTKRPHMEPRTR  
RGPSPPASPTRKPPRLQDFRCLAVLGRGHFGKVLLVQFKGTGKYAIKALKKQEVLSRDE  
IESLYCEKRILEAVGCTGHPFLLSLLVCFQTSSHARFVTEFVPGGDLMMQIHEDVFPEPQ  
ARFYVACVVLGLQFLHEKKIIYRDLKLDNLLLDAAQGLFKIADFGLCKEGIGFGDRTSTFC  
GTPEFLAPEVLTQEAYTQAVDWWALGVLLYEMLVGECPPFGDTEEEVFDCIVNMDAPYPG  
FLSVQGLEFIQKLLQKCPEKRLGAGEQDAEEIKVQPPFRTTNWQALLARTIQPPFVPTLC  
GPADLRYFEGEFTGLPPALTPPAPHSLLTARQQAARDFDFVSERFLEP

SEQ ID NO: 134\_AI021023\_M\_PKNBETA\_M

LKWDNLLLDAAQGLFKIADFGLCKEGIGFGDRTSTFCGTPEFLAPEVLTQEAYTRAVDWWG  
LGVLLYEMLVGECPPFGDTEEEVFDCIVNMDAPYPGFLSVQGLEFIQKLLQKCPEKRLGA  
GEQDAEEIKVQPPFRTTNWQALLARTIQPPFVPTLCGPADLRYFEGEFTGLPPALTPPAP  
HSLLTARQQAARDFDFVSERFLEP

SEQ ID NO: 135\_H19102\_H

GGNIRGPWARGWKS LWTGLGTIRSDLEELWELRGHHYHLHQESLKPAVVLVEKPLPEWPVP  
QFINLFLPEFPPIRPIRGQQQLKILGLVAKGSFGTVLKVLDCTQKAVFAVKVVPKVVLQR  
DTVRQCKEEVSIQRQINHPFVHSLGDSWQGRHLFIMCSYSTDLYSLWSAVGCFPEASI  
RLFAAELVLVLCYLHDLGIMHRDVKMENILLDERGHLKLTDFGLSRHVPQGAQAYTICGT  
LQYMAPEVLSSGGPYNHAADWWSLGVLLFSLATGKFPVAAERDHSVAMLASVTHSDSEIPAS  
LNQGLSLLLHELLCQNPLHRLRYLHHFQVHPFFRGVAFDPELLQKQPVNFVTETQATQPS  
SAETMPFDDFDCDLESFLLYPIFA

## FIGURE 1D

SEQ ID NO: 136\_AA476563\_H

MEFFRIDSKDSASELLGLDFGEKLYSLKSEPLKPFFTLPDGDSASRSFNTSESKVEFKAQ  
DTISRGSDDSVPVISFKDAAFDDVSGTDEGRPDLLVNLPGELESTREAAAAMGPTKFTQTN  
IGIIENKLLLEAPDVLCRLSTEQCQAHEEKGIEELSDPSGPKSYSITEKHYAQEDPRMLF  
VAAVDHSSSGDMSLLPSSDPKFQGLGVVESAVTANNTESLFRICSPLSGANEYIASTDT  
LKTEEVLLFTDQTDLLAKEEPTSLFQRDSETKGESGLVLEGDKEIHQIFEDLDKKLALAS  
RFYIPEGCIQRWAAEMVVALDALHREGIVCRDLNPNILLNDRGHIQLTYFSRWSEVEDS  
CSDSAIERMYCAPEVGAI TEETEACDWWSLGAVLFELLTGKTLVECHPAGINTHTTLNMP  
ECVSEEARSLIQQLLQFNPLERLGAGVAGVEDIKSHPFFTPVDWAELMR

SEQ ID NO: 137\_AA626690\_H

MLPFAPQDEPDREMEVFSGGGASSGEVNGMKMVDEPMEEGEADSCHDEGVVKEIPITHH  
VKEGYEKADPAQFELLKVLGQGSFGKVFLVRKKTGPDAGQLYAMKVLKKASLKVRDRVRT  
KMERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDVFTRLSKEVLFTTEEDVKFYLA  
ELALALDHLHQLGIVYRDLKPENILLDEIGHIKLTD FGLSKESVDQEKKAYSFCGTVEYM  
APEVVNRRGHSQSADWWSYGVLMEMLTGTLPFQKGKDRNETMNMILKAKLGMPQFLSAEA  
QSLLRMLFKRNPANRLGSEGVEEIKRHLFFANIDWDKLYKREVQPPFKPASGKPD DTF CF  
DPEFTAKTPKDSPGLPASANAHQLFKGFSFVATSIAEYKITPITSANVLPVQINGNAA  
QFGEVYELKEDIGVGSYSVCKRCIHATTNMEFAVKIIDKSKRDPSEEIEILMRYGQHPNI  
ITLKDVFDDGRYVYLVTDLMKGGELLDRI LKQKCF SEREASDILYVISKTVDYLHCQGVV  
HRDLKPSNIIYMDESASADSIRICDFGFAKQLRGENG LLLTPCYTANFVAPEVLMQQGYD  
AACDIWSLGVLFYTM LAGYTPFANGPN DTP EEILLRIGNGKFSLSGGNWDNISDGAKDLL  
SHMLHMDPHQRYTAEQILKHSWITHRDQLPNDQPKRNDVSHVVKGAMVATYSALHTKTFQ  
PVLEPVAASSLAQRSMKKRTSTGL

SEQ ID NO: 138\_AA215680\_H

MSLVACECLPSPGLEPEPCSRARSQAHVYLEQIRNRVALGVDPDMTKRDYLVDAATQIRLA  
LERDVSEDEYEA AFNH YQNGVDVLLRGIHVDPNKERREAVKLKITKYLRRAE E I FNCHLQR  
PLSSGASPSAGFSSRLRPIRTLSSAVEQLRGCRVVGVIKVLVQDPATGGTFVVKSLP  
RCHMVSRRERLTII PHGVPMYTKLLRYFVSEDSIFLHLEHVQGGTLWSHLLSQAHSRHSGL  
SSGSTQERMKAQLNPHLNLTPARLP SGHAPGQDRIALEPPRTSPNLL LAGEAPSTRPQR  
EAEGEPTARTSTSGSSDL PKAPGGHLHLQARRAGQNSDAGPPRGLTWVPEGAGPVLGGCG  
RGMDQSCLSADGAGRGCGRATWSVREEQVKQWAAEMLVALEALHEQGVLCRDLHPGNLLL  
DQAGHIRLTYFGQWSEVEPQCCGEAVDNLYS APEVGGISELTEACDWWSFGSLLYELLTG  
MALSQSHPSGIQAHTQLQLPEWLSRPAASLLTELLQFEPTRLGMGEGGVSKLKSHPPFS  
TIQWSKLVG

SEQ ID NO: 139\_SGK\_H

MTVKTEAAKGTLTYSRMGMVAILIAFMKQRRMGLNDFIQKIANNSYACKHPEVQSILKI  
SQPQEPELMNANPSPPPSPSQQINLGPSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKA  
EVFYAVKVLQKKAILKKKEEKHIMSERNVLLKNVKHPFLVGLHFSFQTADKLYFVLDYIN  
GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD  
FGLCKENIEHNSTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSR  
NTAEMYDNILNKPLQLKPNITNSARHLLLEGLLQKDRTKRLGAKDDFMEIKSHVFFSLINW  
DDLINKKITPPFNPVSGPNELRHFDPEFTEEPVPNSIGKSPDSVLVTASVKEAAEAFLG  
FSYAPPTDSFL

SEQ ID NO: 140\_AA107515\_M

MTVKAEEARSTLTYSRMGMVAILIAFMKQRRMGLNDFIQKIASNTYACKHAEVQSILKM  
SHPQEPELMNANPSPPPSPSQQINLGPSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKA

## FIGURE 1E

EVFYAVKVLQKKAILKKKEEKHIMSERNVLLKNVKHPFLVGLHFSFQTADKLYFVLDYIN  
GGELFYHLQRERCFLPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD  
XFQLRRIEHNGTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSRN  
TAEMYDNILNKPLQLKPNITNSARHLLLEGLLQKDRTKRLGAKDDFMEIKSHIFFSLINWD  
DLINKKITPPFNPVSGPSDLRHFDPFTEEPVSSIGRSPDSILVTASVKEAAEAFLGF  
SYAPPVDSFL

SEQ ID NO: 141\_AA109508\_M

HLQRERRFLEPRARFYAAEVASAI<sup>1</sup>GYLHSLNIIYRDLKPENILLDCQGHVVLTDFGLCKE  
GVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSDVSQMY  
ENILHQPLQIPGGRTVAACDLLQSLHKKDQQRQLGSKADFLEIKNHVFFSPINWDDLYHK  
RLTPPFNPNTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPEDDD  
ILDC

SEQ ID NO: 142\_AA887783\_H

MQRDHTMDYKESCPSVXI<sup>1</sup>PSSDEHREKKRFTVYKVLVSVGRSEWFVFRRYAEFDKLYNT  
LKKQFPAXALKIPAKRIFGDNFDPDFIKQRRAGLNEFIQNLVRYPELYNHPDVRAFLQMD  
SPKHQSDPSEDEDERSSQKLHSTSQNINLGPSGNPHAKPTDFDFLKVIGKGSFGKVLLAK  
RKLDGKFYAVKVLQKKIVLNRKEQKHIMAERNVLLKNVKHPFLVGLHYSFQTTEKLYFVL  
DFVNGGEGHVLTDFGLCKEGIAISDTTTTFCGTPEYLAPEVIRKQPYDNTVDWWCLGAV  
LYEMLYGLPPFYCRDVAEMYDNILHKPLSLRPGVSLTAWSI<sup>1</sup>LEELLEKDRQNRLGAKEDF  
LEIQNHPPFFESLSWADLVQKKIPPPFNPVAGPDDIRNFDTAFTTEETVPYSVCVSSDYSI  
VNASVLEADDAFVGFSYAPPS<sup>1</sup>EDLFL

SEQ ID NO: 143\_R47805\_H

MAHQGTGIHATEELKEFFAKARAGSVRLIKVVIEDEQLVLGASQEPVGRWDQDYDRAVLPL  
LDAQQPCYLLYRLDSQNAQGF<sup>1</sup>EWLFLAWSPDNSPVRLKMLYAATRATVKKEFGGGHIKDE  
LFGTVKDDLSFAGYQKHLSSCAAPAPLTS<sup>1</sup>AERELQQIRINEVKTEISVESKHQTLQGLAF  
PLQPEAQRALQQLKQKMVNYIQMKLDLERETIELVHTEPTDVAQLPSRVPRDAARYHFFL  
YKHTHEGDPLESVVF<sup>1</sup>IYSMPGYKCSIKERMLYSSCKSRLLDSVEQDFHLEIAKKIEIGDG  
AELTAEFLYDEVHPKQHAFKQAF<sup>1</sup>AKPKGPGGKRGHKRLIRGPGENGDDS

SEQ ID NO: 144\_H60215\_H

MSKLRMKRRASDRGAGETSARAKALGSGISGNNAKRAGPFILGPRLGNSPVPSIVQCLAR  
KDGTDDFYQLKI<sup>1</sup>LTLEERGDOGIESQEERQGM<sup>1</sup>LLHTEYSLLSLLHTQDGVVHHHGLFQD  
RTCEIVEDTESSRMVKKMKKRICLVLDCLCAHDFSDKTADLINLQHYVIKEKRLSERETV  
VIFYDVVRVVEALHQKNIVHRDLKLGNMVNLNR<sup>1</sup>THRITITNFC<sup>1</sup>LGKHLVSEGDLLKDQRG  
SPAYISPDVLSGRPYRGKPSDMWALGVVLT<sup>1</sup>MTLYGQFPFYDSIPQELFRKIKAAEYTIPE  
DGRVSENTVCLIRKLLVLD<sup>1</sup>PQQR<sup>1</sup>LAAADVLEALS<sup>1</sup>AIASWQSLSSLSG<sup>1</sup>PLQVVPDIDDQM  
SNADSSQEAKVTEEC<sup>1</sup>SQYEFENYMRQQL<sup>1</sup>LLAEKSSI<sup>1</sup>HDTRSWVPKRQFGSAPPVRR<sup>1</sup>LGH  
DAQPMTSLDTAILAQR<sup>1</sup>YLRK

SEQ ID NO: 145\_SGK324\_H

MASTRSIELEHFEERDKRPRPGSRRGAPSSSSGGSSSSSGPKGNGLIPSPAHS<sup>1</sup>AHCSFYRTR  
TLQALSSEKKAKKARFYRNGDRYFKGLVFAISSDRFRSFDALLIELTRSLSDNVNLPQGV  
RTIYTIDGSRKVTS<sup>1</sup>LDELLEGESYVCASNEPFRKVDYTKNINPNWSVNIKG<sup>1</sup>GTSRALAAA  
SSVKSEVKESKDFIKPKLVTVIRSGVKPRKAVRILLNKKTAHSFEQVLT<sup>1</sup>DITEAIKXASG  
VVKRLCTLDGKQVRVTCVHL<sup>1</sup>PDFFGDDDFIACGPEKFRYAQDDFVLDHSECRVLKSSYS  
RSSAVKYS<sup>1</sup>SGSKSPGPSRRSQISAHGRSSSNVNGGPELDR<sup>1</sup>CISPEGVNGNRCSESSTLLEK  
YKIGKVI<sup>1</sup>GDGNFAVVKECIDRSTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNII

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## FIGURE 1F

MLVEEMETATELFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHGLSIVH  
 RDIKPENLLVCEYPDGTSLKLGDFGLATVVEGPLYTVCGTPTYVAPXIIAETGYGLKVD  
 IWAAGVITYILLCGFFPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSAKELISQMLQ  
 VNVEARCTAGQILSHPVVSDDASQENNMQAEVTGKLKQHFNNALPKQNSTTTGVSVMVS  
 GRRQVWPDCGAGLEVFEFGSRELPSHGSWCLP

SEQ ID NO: 146\_W30246\_M SGK324\_M  
 TKSSSSSPTSPGSRGLKISAQGRSSSNVNGGPELDRCLSPGVNGNRCSESFPLLEKYR  
 IGKVIKVDGNFAVVKECVDRYTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNIML  
 VEEMETATDLFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHLSLSIVHRD  
 IKPENLLVCEYPDGTSLKLGDFGLATVVEGPLYTVCGTPTYVAPEIIAETGYGLKVDVW  
 AAGVITYILLCGFPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSPCVCFRKCL

SEQ ID NO: 147\_AA383293\_H  
 PAAKRVVYRNGDPFFPGSQLVVTQRRFPTMEAFLECVTSAVQAPLAVRALYTPCHGHPV  
 TNLADLKNRGQYVAAGFERFHKLPYPYQAFCLSVFRNGDLVSPFFSLKLSQAASQDWETVL  
 KLLTEKVKLQSGAVRLCTLEGLPLSAGKELVTGHYYVAVGEDEFKDLPPALSTRGLLAA  
 GNEAHLRSGVGTVAGSPKPLGRKAKKETCLIVTLTLKYQQSETSRDQGSFSPSGVIGVYGA  
 PHRRKETAGALEVADDEDQTTEEPLDQRAAQIVEQVTCLQDFFGDDDVFIACGPEKFRYA  
 QDDFVLDHSRRRLREHQAGFEKLRRTRGEEKEAEKEKKPCMSGGRMTLRDDQPAKLEK  
 EPKTRPEENKPERPSGRKPRPMGIIAANVEKHYETGRVIGDGNFAVVKECRHRETRQAYA  
 MKIIDKSRLKGKEDMVDSEILIIQSLSHPNIVKLHEVYETDMEIYILILEYVQGGDLFDAI  
 IESVKFPEPDAAALMIMDLCKALVHMHDKSIVHRDLKPENLLVQRNEDKSTTLKLADFGLA  
 KHVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPFRSPXXGDQDE  
 LFNIIQLGHFEFLPPYWDNISDAAKDLVSRLLVVDPPKKRYTAHQVLQHPWIETAGKTNTV  
 KRQKQVSPSSDGHFRSQHKRVVEQVS

SEQ ID NO: 148\_AA197883\_M  
 MPTAPVLRPPPPATPAPPAPSRPAPPIPGHRGPCDHSCLKCLSSKISERKLPGPWLPAGR  
 GPLEKPVLGPRGAVMPLFSPQSSLHSVRAEHSPLKPRVTVVVKLGGQPLRKATLLNRRS  
 VQTFEQLLSDISEALGFPRWKNDVRKLFITLKGREVKSVSDFFREGDAFIAMGKEPLTLK  
 SIQLAMEELYPKNRALALAPHSRVPSRRLRSLPSKLLKGSHRCEAGSYSAEMESKAVS  
 RHQGTSTVLAPEDKARAQKWVRGKQSEPEGGPPSPGAATQEETHASGEKHLGVEIEKTS  
 GEIVRCEKCKRERELQLGLQREPCPLGTSELDLGRAQKRDSEKLVRTKSCRRPSKAKFTD  
 GEEGWKGDShRGSPRDPPEMRRPNSNSDKKEIRGSESQDSYPQGAQKDFVEGPPAV  
 EEGPIDMRREDRHTCRSKHAAWLRREQQAEPPLRTRGEEKQAEHEKKPGGLGERRAPE  
 KESKRKLEEKRPERPSGRKPRPKGIIISADVEKHYDIGGVIGDGNFATVKECRHRETRQAY  
 AMKMIDKSQKKGKEDIVDSEILIIQSLSHPNIVKLHEVYETAEIYLIMEYVQGGDLFDA  
 IVENVKFPEPEAAVMITDLCKAFVHMHDKNIVHRDVKPENLLVQRNEDKSITLKLADFG  
 AKYVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPFRSPERDQDE  
 LFNIIQVQGFELSPYWDNISDAAKDLVRNLLVDPKKRYTAEQVLQHPWIEMVGHTNTG  
 NSQKEESPNSLGHFQSQHKKVAEQMP

SEQ ID NO: 149\_DRAK2\_H  
 MSRRRFDCRSISGLLTTPQIIPIKMFNNFYILTSKELGRGKFAVVRQCISKSTGQEYA  
 AKFLKKRRRGQDCRAEILHEIAVLELAKSCPRVINLHEVYENTSEIILILEYAAGGEIFS  
 LCLPELAEMVSENDVIRLIKQILEGVYYLHQNNIVHLDLKPQNILLSSIYPLGDIKIVDF  
 GMSRKIGHACELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN  
 QETYNISQVNVDYSEETFSSVSQLATDFIQSLLVKNPEKRPTAEICLSHSWLQOWDFEN

## FIGURE 1G

LFHPEETSSSSQTQDHSVRSSSEDKTSKSSCNGTCGDREDKENI PEDSSMVSKRFRFDDSL  
PNPHELVSDLCLC

SEQ ID NO: 150\_W44160\_M DRAK2\_M  
MSRRRFDRCRSVSGLLTTTPQTPIKTENFNFFYTLTPKELGRGKFAVVRQCISKSTGQEYA  
AKSLKKRRRGQDCRAEILHEIAVLELARSCHVINLHEVYENATEIILVLEYAAGGEIFN  
LCLPELAEMVSENDVIRLIKQILEGVHYLHQNNIVHLDLKPQNILLSSYPLGDIKIVDF  
GMSRKIGNASELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN  
QETYNISQVNVVDYSEEMFSSVSQLATDFIQSLLVKNPEKRPTAESCLSHSWLQQWDFGS  
LFHPEETSGSSQIQDLTLRSSEEKTSKSSCNGSCGAREDKENI PEDGSLVSKRFRFDDSL  
PSPHELVPDFLC

SEQ ID NO: 151\_H01248\_H, DRAK1\_H  
MIPLEKPGSGGSSPGATSGSGRAGRGLSGPCRP PPPPPQARGLLTEIRAVVRTEPFQDGYS  
LCPGRELGRGKFAVVRKCIKKDSGKEFAAKFMRKRRKGQDCRMEIHEIAVLELAQDNPW  
VINLHEVYETASEMILVLEYAAGGEIFDQCVADREEAFKEKDVQRLMRQILEGVHFLHTR  
DVVHLDLKPQNILLTSESPLGDIKIVDFGLSRILKNSEELREIMGTPEYVAPEILSYDPI  
SMATDMWSIGVLTYVMLTGISPFLGNDKQETFLNISQMNLSYSEEEFDVLSESAVDFT  
LLVKKPEDRATAEECLKHPWLTQSSIQEPSFRMEKALEEANALQEGHSVPEINSDTDKSE  
TEESIVTEELIVVTSYTLGQCRQSEKEKMEQKAIKSRFKFEEPLLQEIPGEFIY

SEQ ID NO: 152\_AA021445\_H  
MPARIGYYEIDRTIGKGNFAVVKRATHLVTKAKVAIKIIDKTQLDEENLKKIFREVQIMK  
MLCHPHIIRLYQVMETERMIYLVTEYASGGEIFDHLVAHGRMAEKEARRKFKQIVTAVYF  
CHCRNIVHRDLKAENLLLDANLNKIAADFGFSNLTFTPGQLLKTWCGSPPYAAPELFEGKE  
YDGPVKVDIWSLGVVLYVLVCGALPFDGSTLQNLRLARVLSGKFRI PFFMSTECEHLIRHML  
VLDPNKRLSMEQICKHKWMKLGADDPNFDRLIAECQQLKEERQVDPLNEDVLLAMEDMGL  
DKEQTLQSLRSDAYDHYSAIYSLLCDRHKRHKTLLRGALPSMPRALAFQAPVNIQAEQAG  
TAMNISVPQVQLINPENQIVEPDGTLNLDSDGEDEEPSPEALVRYLSMRRTVGVADPRTE  
VMEDLQKLLPGFPGVNPQAPFLQVAPNVNFMHNLPLMQNLQPTGQLEYKEQSLLQPPTLQ  
LLNGMGPLGRRASDGGANIQLHAQQLLKRPRGPSPLVTMTPAVPAVTPVDEESSDGEPOQ  
EAVQRYLANRSKRHTLAMTNPTAEIPPDQLRQLGQQPFRSRVWPPHLVPDQHRSTYKDSN  
TLHLPTERFSPVRRFSDGAASIQAFKAHLEKMGNNSSIKQLQQECEQLQKMYGGQIDERT  
LEKTQQQHMLYQQEQHHQILQQQIQDSICPPQPSPLQAACENQPALLTHQLQRLRIQPS  
SPPPNHPNNHLFRQPSNSPPPMSSAMIQPHGAASSSQFQGLPSRSAIFQQQPENCSSPPN  
VALTCLGMQQPAQSQQVTIQVQEPVDMLSNMPGTAAGSSSGRGISISPSAGQMOMQHRTNL  
MATLSYGHRPLSKQLSADSAEASHLVNVRFPANYDQAHLPPLHFLSDQSRGSPSSYSPST  
GVGFSPTQALKVPPLDQFPTFPFSAHQPPHYTTALQQALLSPTPPDYTRHQQVPHILQ  
GLLSPRHSLTGHSIDIRLPPTFEAQLIKRQQQQRQQQQQQQQQQEYQELFRHMNQGDAGSL  
APSLGGQSMTERQALSQYQADSYHHHTSPQHLLQIRAEQCVSQASSPTPPHGYAHQPALM  
HSESMEECDSCGAKDGFQDSKSSSTLTGCHDSPLLLSTGGPGDPESLLGTVSHAQELG  
IHPYGHQPTAAFSKNKVPSPREPVI GNCMDRSSPGQAVELPDHNGLGYPARPSVHEHHRPR  
ALQRHHTIQNSDDAYVQLDNLPGMSLVAGKALSSARMSDAVLSQSSLMGSQQFQDGENEE  
CGASLGGEHPDLSDGSQHLNSSCYPSTCITDILLSYKHPEVSFSMEQAGV

SEQ ID NO: 153\_2R22-5-11\_H  
MTAVYMNGGGLVNPHYARWDRRDSVESGCQTESSEKEGEGQPRQLTPFEKLTQDMSQDEK  
VVREITLGRIGFYRIRGEIGSGNFSQVKLGHSILTKEKVAIKILDKTKLDQKTQRLLSR  
EISSMEKLHHPNIIIRLYEVVETLSKLHLVMEYAGGGELFGKISTEGLSEPESEKLIIFSQI  
VSAVKHMHENQIIHRDLKAENVFYTSNTCVKVGDFGFSTVSKKGEMLNTFCGSPPYAAPE

## FIGURE 1H

LFRDEHYIGIYVDI WALGVLLYFMVTGTM PFRAETVAKLKKSILEGTYSVPPHVSEPCHR  
LIRGVLQQIPTERYGIDCIMNDEWMQGVPTPTLEPFQLDPKHLSETSTLKEEENEVKST  
LEHLGITEEHIRNNQGRDARSSITGVYRIILHRVQRKKALESVPVMMLPDPKERDLKKGS  
RVYRGIRHTSKFCSIL

SEQ ID NO: 154\_R31237\_1\_H, AAC33487

MSTRTP LPTVNERDTENHTSHGDGRQEVTSRTSRSGARCRNSIASCAD EQPHIGNYRL LK  
TIGKGNFAKVKLARHILTGREVAIKIIDKTQLNPTSLQKLFREVRIMKILNHPNIVKLFE  
VIET EKTLYLIMEYASGG EVFDYLV AHGRMKEKEARSKFRQIVSAVQYCHQKRIVHRDLK  
AENLLLDADMNIKIADFGFSNEFTVGGKLDTF CGSPPYAAPELFQGGKYDGP EVDVWSLG  
VILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTDCENLLKRFLVLNPIKRG TLEQ  
IMKDRWINAGHEEDELKPFVEPELDISDQKRIDIMVGMGYSQEEIQESLSKMKYDEITAT  
YLLGRKSSSELDASDSSSSSNLSLAKVRPSSDLNNSTGQSPHHKVQRSVSSSQKQRRYS  
HAGPAIPSVVAYPKRSQTSTADGDLKEDGISSRKSSGSAVGKG IAPASPMLGNASPNK  
ADIPERKKSSTVPSSNTASGGMTRNTYVCSERTTADRHSVIQNGKENSTIPDQRTPVAS  
THS ISSAATPDRI RFPRGTASRSTFHGQPRERRTATYNGPPASPSLSHEATPLSQTRSRG  
STNLF SKLTSKLTRSRNVSAEQKDENKEAKPRSLRFTWSMKTTSMDPGDMMREIRKVLD  
ANNC DYEQRERFLLFCVHGDGHAENLVQWEMEVC KLPRLSLNGVRFKRISGTSIAFKNIA  
SKIANELKL

SEQ ID NO: 155\_W90839\_M

KGPSWSSRSLGARCRNSIASCPEEQPHVGN YRLLRITIGKGNFAKVKLARHILTGREVAIK  
IIDKTQLNPSSLQKLFREVRIMKGLNHPNIVKLFEVIET EKTLYLVMEYASAGEVFDYLV  
SHGRMKEKEARAKFRQIVSAVHYCHQKNIVHRDLKAENLLLD AEANIKIADFGFSNEFTL  
GSKLDTF CGSPPYAAPELFQGGKYDGP EVDIWSLG VILYTLVSGSLPFDGHN LKELRERV  
LRGKYRVPFYMSTDCESILRRFLVLNPAKRCTLEQIMKDKWINIGYEGEELKPDTELKEE  
RMPGRKASCSAVGSGSRGLPPSSPMVSSAHNPNAEIPERRKDSTSTPNNLPSSMMTRRN  
TYVCTERPGSERPSLLPNGKENSSGTSRVPPASPSHSLAPPSGERSRLARGSTIRSTFH  
GGQVRDRRAGSGSGGGVQNGPPASPTLAHEAAPLP SGRPRPTTNLFTKLTSKLTRRV TDE  
PERIGGPEVTSCHLPWDKTETAPRLLRFPWSVKLTSSRPS

SEQ ID NO: 156\_406786.5\_H

MEVGGLTVFEEDQRCLSQSLPLPVSAEGPAAQTAEPSRSFSSAHRHLSRRNGLSRLCQS  
RTALSEDRWSSYCLSSLAQNICTSKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSSGWSS  
PLLPAPVCNPNAKIFTVDAKTTEILVANDKACGLLGYSQDLIGQKLTQFFLRSDSDVVE  
ALSEEHMEADGHAAVVFGTVVDIITRSGEKIPVSVWMKMRQERRLCCVVVLEPVERVST  
WVAFQSDGTITSCDSLFAHLHGYVSGEDVAGQHITDLIPSVQLPPSGQHIPKNLKIQRSV  
GRARDGTTFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLPDGTI HGI  
NHSFALT LFGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNESGCGER  
TLDPWQGGQDPAEGGQDPRINVVL AGGHVVRDEIRKLME SQDIFTGTQTELIAGGQLLSC  
LSPQPAPGVDNVPEGSLPVHGEQALPKDQQIT ALGREEPVAIESPGQDLLGESRSEPVDV  
KPFASCEDSEAPVPAEDGGS DAGMCGLCQKAQLERMGVSGPSGSDLWAGAAVAKPQAKGQ  
LAGGSLLMHCPCYGSEWGLWWSQDLAPSPSGMAGLSFGTPTLDEPWLG VENDOR EELQTC  
LIKEQLSQLSLAGALDVPHAELVPTECQAVTAPVSSCDLGGRDLCGGCTGSSSACYALAT  
DLPGGLEAVEAQEVDVNSFSWNLKELFFSDQTDQTSSNCSCATSELRETPSSLA VGSDPD  
VGS LQE QGSCVLD DRELLLLTGTCVDLGQGRRFRESCVGHDPTEPLEVCLVSSEHYAASD  
RESPGHVPSTLDAGPEDTCPSAEPEPRLNVQVTSTPVI VMRGAAGLQREIQEGAYSGSCYH  
RDGLRLSIQFEVRRVELQGPTPLFCCWL VKDLLHSQRDSAARTRFLASLP GSTHSTAAE  
LTGPSLVEVLRARPWFEEPPKAVELEGLAAC EGEYSQKYSTMSPLGSGAFGFVWTA VDKG  
KNKEVVVKFIKKEKVLED CWIEDPKLGKVTLEIAILSRVEHANI I KVLDI FENQGGFFQLV

## FIGURE 11

MEKHGSGLDLFAFIDRHPRLDEPLASYIFRQVRAGQSRLVSAVGYLRLKDI IHRDI KDEN  
 IVIAEDFTIKLIDFGSAAYLERGKLFYTFCTIEYCAPEVLMGNPYRGPELEMWSLGVTL  
 YTLVFEENPFCELEETVEAAIHPPYLVSKELMSLVSGLLQPVPERRTTLEKLVTDPWVTQ  
 PVNLADYTWEVFRVKNKPESGVLSAASLEMGNRSLSDVAQAQELCGGPVPGAPNGQGCL  
 HPGDPRLLTS

SEQ ID NO: 157\_AA544838\_M 406786\_M

TRPHPCLEPLASFI FRQLVSAVGYLHSQGI IHRDI KDENIVIAEDFTIKLIDFGSAAYL  
 ERGKLFYTFCTIEYCAPEVLIGNPYRGPELEMWSLGVTLTYTLIFEENPFCEVEETMEAV  
 IHPPFLVSQELMSLLSGLLQPCPEQRTTLEKLIRDPWVTQPVNLASYTWEVCRNTNQPS  
 GLLSAASLEIGSRSPSEMAQREGLCGPPAPRETRGDQHCLHLKDPSLPVS

SEQ ID NO: 158\_AA785735\_H

MVMADGPRHLQRGPPVRVGFYDIEGTLGKGNFAVVKLGRHRITKTEVAIKI IDKSQLDVN  
 LEKIYREVQIMKMLDHPHI IKLYQVMETKSMLYLVTYAKNGEIDYLANHGRLNESEAR  
 RKFWQILSAVDYCHGRKIVHRDLKAENLLLDNNMIKIADFGFGNFFKSGELLATWCGSP  
 PYAAPEVFEGQQYEGPQLDIWSMGVVLYVLVCGALPFDGPTLPILRQRVLEGRFRI PYFM  
 SEDCEHLIRRLVLDPKRLTIAQIKEHKWMLIEVPVQRPVLYPQEQENEPSIGEFNEQV  
 LRLMHS LGIDQQKXIESLQNKSYNHFAAIYFLLVERLKSHRSSFPVEQRLDGRQRRPSTI  
 AEQTVAKAQTVGLPVTMHS PNMRLLSALLPQASNVEAFSFPASGCQAEAAFMEEECVDT  
 PKVNGCLLDPPVPVLVRKGCQSLPSNMMETSIDEGLETEGEAEEDPAHAFAEFQSTRSGQ  
 RRHTLSEVTNQLVVMGAGKIFSMNDSPSLDSVDSEYDMGSVQRDNLNLEDNPSLKDIML  
 ANQPSPRMTSPFISLRPTNPAMQALSSQKREVNHRSPVS FREGRRASDTSLTQGI VAFRQ  
 HLQNLARTKGILELNKVQLLYEQIGPEADPNLAPAAPQLQDLASSCPQEEVSQQQESVST  
 LPASVHPQLSPRQSLETQYLQHRLOKPSLLSKAQNTCQLYCKEPPRSLEQQQLQEHRLQOK  
 RLFLQKQSQLQAYFNQMQUIAESSYPQPSQQLPLPRQETPPPSQQAPPFSLTQPLSPVLEP  
 SSEQMQYSPFLSQYQEMQLQPLPSTSGPRAAPPLPTQLQQQQPPPPPPPPPPRQPGAAPA  
 PLQFSYQTCELPSAASPAPDYPTPCQYPVDGAQQSDLTGPDCPRSPGLQEAPSSYDPLAL  
 SELPGLFDCEMLDAVDPQHNGYVLVN

SEQ ID NO: 159\_AA207220\_H

MESLVFARRSGPTPSAAELARPLAEGLIKSPKPLMKKQAVKRHHHKHNLRRHYEFLETG  
 KGTYGKVKKARESSGRLVAIKSIRKDKIKDEQDLMHIRREIEIMSSLNHPHIIAIEHVFE  
 NSSKIVIVMEYASRGDLYDYISERQQLSEREARHFFRQIVSAVHYCHQNRVVRDLKLEN  
 ILLDANGNIKIADFGLSNLYHQGKFLQTFCSPLYASPEIVNGKPYTGPEVDSWSLGVLL  
 YILVHGTMPFDGHDHKILVKQISNGAYREPPKPSDCLXGLIRWLLMVNPTRRATLEDVAS  
 HWWVNWGYATRVGEQEAPHEGGHPSGDSARASMAWLRSSRPLENGAKVCSFFKQHAP  
 GGGSTTPGLERQHS LKSRKENDMAQSLHSDTADDTAHRPGKSNLKL PKGILKKKVSASA  
 EGVQEDPPELSPIPASPGQAAPLLPKKGILKKPRQRESGYYSPEPSES GELL DAGDVV  
 SGDPKEQKPPQASGLLLHRKGILKLNGKFSQTALELAAPTTFGSLDELAPPRPLARSRP  
 SGAVSEDSILSSSEFDQLDLPERLPEPPLRGCVSDNLTGLEPPSEGGPGSCLRRWRQDP  
 LGDSCFSLTDCQEVATATYRQALRVCSKLT

SEQ ID NO: 160\_AA426580\_H, MAK\_V\_H

MPAAAGDGLLGEPAPGGGGGAEDAARPAACEGSFLPAWVSGVPRERLRDFQHKKRVGN  
 YLIGSRKLGECSFAKVREGLHVLTKGEKVAIKVIDKKRAKDTYVTKNLRREGQIQQMIRH  
 PNITQLLDILETENSYYLMELCPGGNLMHKIYEKKRLEESEARRYIRQLISAVEHLHRA  
 GVVRDLKIEENLLLEDNNIKLIDFGLSNCAIGLYSDPFSTQCGSPAYAAPELLARKKY  
 GPKIDVWSIGVNMYAMLTGTLPTTVEPFSRLALYQKMVDKEMNPLPTQLSTGAISFLRSL  
 LEPDPVKRPNIQQALANRWLNENYTGKVPCNVTPNRISLEDLSPSVVLHMTEKLGKNS

## FIGURE 11

DVINTVLSNRACHILAIYFLINKKLERLYLSGKSDIQDSLQYKTRLYQIEKYRAPKESYEA  
SLDTWTRDLEFHAVQDKKPKEQEKRGDFLHRPFSKKLDKNLPSHKQPSGSLMTQIQNTKA  
LLKDRKASKSSFPDKDSFGCRNIFRKTSDSNVASSSMEFIPVPPRTPRIVKKPEPHQF  
GPGSTGIPHKEDPLMLDMVRSFESVDRDDHVEVLSPSHHYRILNSPVSLARRNSSERTLS  
PGLPSGSMSP LHPTLHPTLVSF AHEDKNSPPKKEGLCCPPPVPSNGPMQPLGSPNCVKSR  
GRFPMGIGQMLRKRHQS LQPSADRPLEASLPPLQPLAPVNLA FDMADGVKTQC

SEQ ID NO: 161\_Z36720\_H

MDTKLNMLNEKVDQLLHFQEDVTEKLQSMCRDMGHLEGLHRLEASRAPGPGGADGVPHI  
DTQAGWPEVLELVRAMQQDAAQHGARLEALFRMVA AVDRAIALVGATFQKSKVADFLMQG  
RVPWRRGSPGDSPEEWVKEEEVCFMPPVPPAPGAAGQSLQDKGELS AEQGIWATLMTLV  
IMVTAANKERVEEEGGKPKHVLSTSGVQSDAREPGEESQKADVLEGTAERLPPIRASGLG  
ADPAQAVVSPGQGDGVP GPAPQAFPGHLPLPTKVEAKAPETPSENLR TGLELAPAPGRVNV  
VSPSLEVAPGAGQGASSSRPDPEPLEEGTRLT PGPGPQC PGPPGLPAQARATHSGGETPP  
RAALLKGAVAPGFSRRDLVFPSIFCACLGISIHIQEMDTPGEMLM TGRGSLGPTLTTEAP  
AAAQPGKQGPPGTGRCLQAPGTEPGEQTPEGARELSPLQESSSPGGVKAEEEQRAGAEFG  
TRPSLARSDDDNDHEVGALGLQQGKSPGAGNPEPEQDCAARAPVRAEAVRRMPPGAEGSV  
VLDDSPAPPAPFEHRVSVKETSISAGYEVQCHEVLGGGRFGQVHRCTEKSTGLPLAAKI  
IKVKSADREDVKNEINIMNQLSHVNLIQLYDAFESKHSCTLVMEYVDGGELFDRITDEK  
YHLTELDVVLFTTRQICEGVHYLHQHYILHLDLKPENILCVNQTGHQIKI IDFG LARRYKP  
REKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVG VITYMLLSGLSPFLGETDAETMNFIV  
NCSWDFDADTFEGLSEEAKDFVSRLLVKEKSCRMSATQCLKHEWLNNLPKASRSKTRLK  
SQLLLQKYIAQRKWKKH FYVVTAANRLRKFTSP

SEQ ID NO: 162\_SGK088\_H

GEMALFECLVAGPTDVEVDWL CRGRLLPALLKCKMHFDGRKCKLLLT SVHEDDSGVYTC  
KLSTAKDELTC SARLTVRPSLAPLFTRLLEDVEVLEGRAARFDCKI SGT PPPVVTWTHFG  
CPMEESENRLRQDGGLHSLHIAHV GSEDEGLYAVSAVNTHGQAHCSAQLYVEEPRTAAS  
GPSSKLEKMP SIPEEPEQGELERLSIPDFLRPLQDLEVGLAKEAMLECQVTGLPYPTISW  
FHNGHRIQSSDDRRMTQYRDVHRLVFP AVG PQHAGVYKSVIANKLGAACYAHLYVTDVV  
PGPPDGAPQVVAVTGRMVTLTWNPPRSLDMAIDPDSLTYTVQH QVLGSDQWTALVTGLRE  
PGWAATGLRKG VQHI FRVLSTTVKSSSKPSPSEP VQLLEHGPTLEEAPAMLDKPDIVYV  
VEGQPASVTVT FNHVEAQVWVRSCRGALLEARAGVYELS QPDDDQYCLRICRVSRDMGA  
LTCTARNRHGTQTCSVTLELAEAPRFESIMEDVEVGAGETARFAVVVEGKPLPDIMWYKD  
EVLLTSSHVSVFVYEENEC SLVVLSTGAQDGGVYTCTAQN LAGEVSCAE LAVHSAQTAM  
EVEGVGEDEDHRGRRLSDFYDIHQEI GRGAFSYLRRI VERSSGLEFAAKFI PSQAKPKAS  
ARREARLLARLQHDCVLYFHEAFERRRGLVIVTELCTEELLER IARKPTVCESEIRAYMR  
QVLEGIHYLHQSHVLHLDVKPENLLVWDGAAGEQQVRI CDFGNAQELTPGEPQYCYGTP  
EFVAPEIVNQSPVSGVTDIWPVGVAFLCLTGISPFVGENDR TTLMNIRNYNVAFEETTF  
LSLSREARGFLIKVLVQDRLRPTAEETLEHPWFKTQAKGAEVSTDHLKLF LSRRRWQRSQ  
ISYKCHLVLRPIPELLRAPPERVWVTMPRRPPPSGGLSSSSDSEEEEELEELPSVPRPLQP  
EFGSRSVSLTDIPTED EALGTPETGAATPMDWQEQGRAPSQDQEAPSPEALPSPGQEPAA  
GASPRRGELRRGSSAESALPRAGPRELGRGLHKAASVELPQRRSPGPGATRLARGGLGEG  
EYAQRLQALRQRLLRGGPEDGKVSGLRGPLLES LGGRARDPRMARAASSEAPPHQPPLE  
NRGLQKSSSF SQGEAEPRGRHRRAGAPLEIPVARLGARRLQESPSLSALSEAQPSSPARP  
SAPKPSTPKSAEPSATT PSDAPQPPAPQPAQDKAPEPRPEPVRASKPAPPQALQTLALP  
LTPYAQIIQSLQLSGHAQGPSQGPAAAPPSEPKPHAAVFARVASPPPGAPEKRVPSAGGPP  
VLAEKARVPTVPPRPGSSSLSSSIENLESEAVFEAKFKRSRESPLSLGLRLLSRSRSEERG  
PFRGAEEEDGIYRPS PACTPLELVRRPERSRSVQDLRAVGEPGLVRRLSLSLSQRLRRTF  
PAQRHPAWEARGGDGESSEGGSSARGSPVLAMRRRLSFTLERLSSRLQRSGSSED SGGAS



## FIGURE 1K

GRSTPLFGRRLRRATSEGESLRRRLGLPHNQLAAQAGATTPSAESLGSEASATSGSSAPGES  
RSRLRWGFSRPRKDKGLSPPNLSASVQEELGHQYVRSESDFPVFHIIKLKDQVLLGEAA  
TLLCLPAACPAPHISWMKDKKSLRSEPSVIVSCKDGRQLLSIPRAGKRHAGLYECSATN  
VLGSITSSCTVAVARVPGKLAPPEVTQTYQDTALVLWKPGDSRAPCTYTLERRVDGESVW  
HPVSSGIPDCYYNVTHLPVGVTVRFRVACANRAGQGPFSSNSSEKVFVRGTQDSSAVPSAA  
HQEAPVTSRPARARPPDSPTSLAPPLAPAAPTPPSVTVSPSSPPTPPSQALSSSLKAVGPP  
PQTPRRRHRGLQAARPAEPTLPSTHVTPSEPKPFVLDGTPIIPASTPQGVKPVSSSTPVY  
VVTSFVSAPPAPEPPAPEPPPEPTKVTVQSLSPAKEVVSSPGSSPRSSPRPEGTTLRQGP  
PQKPYTFLEEKARGRFGVVRACRENATGRTFVAKIVPYAAEGKPRVLQEYEVRLTLHHER  
IMSLHEAYITPRYLVLIAESCGNRELLCGLSDRFYSEDDVATYMVQLLQGLDYLHGHV  
LHLDIKPDNLLLAPDNALKIVDFGSAQPYNPQALRPLGHRTGTLEFMAPEMVKGEPIGSA  
TDIWGAGVLTYYIMLSGRSPFYEPDPQETEARIVGGRFADFQLYPNTSQSATLFLRKVLSV  
HPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRRAEAATRHKVLLR  
SYPGGP

SEQ ID NO: 163\_AA542015\_M SGK088\_M  
ATDIWGAGVLTYYIMLSGYSPFYEPDPQETEARIVGGRFADFQLYPNTSQSATLFLRKVLS  
VHPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRRAEAATRHKVLL  
RSYPGSP

SEQ ID NO: 164\_R19772\_H  
MKGGDRAYTRGPSLGWLFACCCCCFPCRDAYSHTSSSENGGKSESVANLQAQPSLNFIHSS  
PGPKRSTNTLKKWLTSPVRLNSGKADGNIKKQKKVRDGRKSFDLGSPKPGDETTPQGD  
ADESKKGWGEDEPDEESHTPLPPPMKIFDNDPTQDEMSSSLAARQASTEVPATAADLVNA  
IEKLVKNKLSLEGSSYRGLKDPAGCLNEGMAPPTPKNPPEEQKAKALRGRMFVLNELV  
QTEKDYVKDLGIVVEGFMKRIEEKGVPEDMRGKDKIVFGNIHQIYDWHKDFFLAELEKCI  
QEODRLAQLFIKHERKLHIYVWYCQNKPRSEYIVAEYDAYFEEVKQEIINQRLTSLDFLIK  
PIQRITKYQLLLKDFLRYSEKAGLECSDIEKAVELMCLVPKRCNDMMNLGRLQGFEGTLT  
AQQKLLQQDTFYVIELDAGMQSRTKERRVFLFEQIVIFSELLRKGSALTPGYMFKRSIKMN  
YLVLEENVNDNDPCKFALMNRETSEVVVLOANADIQQAWVQDINQVLETQRDFLNALQSP  
IEYQRKERSTAVMRSQPARLPQASPRPYSSVPAGSEKPPKGSSYNPPLPLKISTNSGSP  
GFEYHQPGDKFEASKNDLGGCNGTSSMAVICKDYALKENEICVSQGEVVQVLAVNQNMCMC  
LVYQPASDHSPAAEGWVPGSILAPLTKATAAESDGSIKKSCSWHTLRMRKRAEVENTGK  
NEATGPRKPKDILGNKVSVKETNSSESECDLDPNTSMELNPNFIQEVAPFLVPLVD  
VTCLLGDTVILQCKVCGRPKPTITWKGPQDQNILDTDNSSATYTVSSCDSGEITLKI CNLM  
PQDSGIYTCIATNDHGTSTSATVKVQGVPAAPNRPPIAQERSCTSVILRWLPPSSTGNCT  
ISGYTVEYREEGSQIWQQSVASTLDTYLVIEDLSPGCPYQFRVSASNPGWISLPSEPSEF  
VRLPEYDAAADGATISWKENFDSAYTELNEIGRGRFSIVKKCIHKATRQDVAVKFVNKKM  
KKKEQAHEAALLQHLQHPQYITLHDTYESPTSIIILILELMDDGRLLDYLMNHDELMEEK  
VAFYIRDIMEALQYLHNCRVAHLDIKPENLLIDLRI PVPRVKLIDLEDAVQISGHFHH  
LLGNPEFAAPEVIQGI PVSLGTDIWSIGVLTYYMLSGVSPFLDESKEETCINVCRVDFSF  
PHEYFCGVSNAARDFINVLQEDFRRRPTAATCLQHPWLQPHNGSYSKIPLDTSRLACFI  
ERRKHQNDVRPIPNVKSIIVNRVNQGT

SEQ ID NO: 165\_5R72\_8\_2\_H  
MADSGLDKKSTKCPDCSSASQKDVLCVCSSKTRVPPVLVVEMSQTSSIGSAESLISLERK  
KEKNINRDITSRKDLPSRTSNVERKASQQWGRGNFTEGKVPHIRIENGAAIEEIIYTFGR  
ILGKGSFGIVIEATDKETETKWAIIKKVNKEKAGSSAVKLLEREVNILKSVKHEHIIHLEQ  
VFETPKKMYLVMELCEDGELKEILDRKGHFSENETRWWIIQSLASAIAYLHNNDIVHRDLK  
LENIMVKSSLI DDNNEINLNIKVTD FGLAVKKQSRSEAMLQATCGTPIYMAPEVISAHDY

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## FIGURE 11.

SQQCDIWSIGVVMYMLLRGEPPFLASSEAKLFELIRKGELHFENAVVNSISDCAKSVLKQ  
LMKVDPAHRI TAKELLDNQWLTGNKLSSVRPTNVLEMMKEWKNNPESVEENTTEENKPS  
TEEKLSYQPWGNVPETNYTSDEEEEEKQSTAYEKQFPATSKDNFDMCSSSFTSSKLLPAE  
IKGEMEKTPTVTPSQGTATKYPAKSGALSRTKKKL

SEQ ID NO: 166\_SGK309\_H

MQCLAAALKDETNMSSGGGEQADILPANYVVKDRWKVLKKIGGGGFGEIYEAMDLLTRENV  
ALKVESAAQQPKQVLKMEVAVLKKLQGSGLGQGDGKEEMMKPGAKRGKDHVCRFIGCGRNE  
KFNYVVMQLQGRNLADLRRSQPRGTFTLSTTLRLGKQILESIEAIIHSGVGLHRDIKPSNF  
AMGRLPSTYRKCYMLDFGLARQYTNTTGDVPRPNVAGFRGTVRYASVNAHKNREMGRHD  
DLWSLFYMLVEFAVGQLPWRKIKDKEQVGMKEKEYEHRMLLKHMPSSEFHLFLDHIASLDY  
FTKPDYQLIMSVFENSMKERGIAENEAFDWEKAGTDALLSTSTSTPPPAEHPADGSHVWG  
GQCDASAWGPAPGEHRCATGRAPEXPGECTPNSAREALXGAGPQSPPCPPPRGSXGXSL  
GGDRCQPEQTPDQHRQSNCRQGEGRGWPFLLSPPIPSLVPLPCSSXAPCPPPISLLARPLF  
PVPSPALASLCLPSSSSSVSFTLRRPSA

SEQ ID NO: 167\_AA234451\_H

MSGGGEQLDILSVGILVKERWKVLRKIGGGGFGEIYDALDMLTRENVALKVESAAQQPKQV  
LKMEVAVLKKLQGDHVCRFICGGRNDRFNYYVMQLQGRNLADLRRSQSRGTFTISTTLR  
LGRQILESIESIHSVGSXHRDIKPSNFMAGRFPSTCRKCYMLDFGLARQFTNSCGDVRRP  
RAVAGFRGTVRYASINAHNRNREMGRHDDLWSLFYMLVEFVVGQLPWRKIKDKEQVGSIKE  
RYDHRMLMLKHLPPFSIFLDHISLDYFTKPDYQLLTSVFDNSIKTFGVIESDPFDWEKT  
GNDGSLTTTTTSTTPQLHTRLTPAAIGIANATPIPGDLLRENTDEVFPDEQLSDGENGIP  
VGVSPDKLPGSLGHPRPQEKDVWEEMDANKNKIKLGIKKAATEEENSHGQANGLLNAPSL  
GSPIRVRSEITQPDREDIPLVRKLRSIHSFELEKRLTLEPKPDTDKFLETWYKIVYFSF

SEQ ID NO: 168\_AA435956\_H

TFTIFFEMTVFDLEAKSARGGSNLLMDSVSSFQLFMFQLLRGLAYIHHQHVLHRDLKPQN  
LLISHLGELKLADFLARAKSIPSQTSSEVVTLWYRPPDALLGATEYSSELDIWGAGCI  
FIEMFQGGPLFPGVSNILEQLEKIWEVLGVPTEDTWPVGVSCLPNYNPEWFPLPTPRSLHV  
VWNRLGRVPEAEDLASQMLKGFPRDRVSAQEALVHDYFSALPSQLYQLPDEESLFTVSGV  
RLKPEMCDLLASYQKGHPAQFSKCW

SEQ ID NO: 169\_AA626859\_H

NGVADGVIKSVLWQTLQALNFCHIHNCIHRDIKPENILITKQGIKICDFGFAQILIPGD  
AYTDYVATRWRAPPELLVGDTQYGSSVDIWAIGCVFAELLTGQPLWPGKSDVDQLYLIIR  
TLGKLI PRHQSIFKSNGFFHGISIPEPEDMETLEEKFSVHPVALNFMKGCLKMNPDDR  
TCSQLLESSYFDSFQEAQIKRKARNEGRNRRRQQNQQLLPLIPGSHISPTPDGRKQVLQK  
FDHLPNI

SEQ ID NO: 170\_AA061797\_M

KIALREIRMLKLKHPNLVNLIEVFRKRKMHLVFEYCDHTLLNELERNPNGVSDGVIKSV  
LWQTLQALNFCHKHNCIHRDVKPENILITKQGMIKICDFGFARILIPGDAYTDYVATR  
WRAPPELLVGDTKYGSSVDVWAVGCVFAELLTGQPLWPGKSDVDQLYLIIRTLGKLI  
PRHQSIFRSNQFFRGISIPEPEDMETLEEKFSNVQPVALSFMKGCLKMNPDERLTCAQL  
LDSAYFESFQEDQMKRKARSEGRSRRRQQNQQLLPLIPGSHISPTPDGRKQVVLKFDHLPNI

SEQ ID NO: 171\_AA397553\_H

MPNSERHGGKKDGS GGASGTLPSSGGSSNSRERHRLVSKHKRHKSKHSDMGLVTPEA  
ASLGTVIKPLVEYDDISSDSDTFSDDMAFKLDRRENDERRGSDRSDDLHKHRRHQHRRSR

## FIGURE 1M

DLLKAKQTEKEKSQEVSSKSGSMKDRI SGSSKRSNEETDDYGKAQVAKSSSKESRSSSKLH  
 KEKTRKERELKSGHKDRSKSHRKRETPKSYKTVDSPKRRSRSPHRKWSDDSSKQDDSPSGA  
 SYGQDYDLSPSRSHSTSSNYDSYKKSPGSTSRQSVSPPYKEPSAYQSSTRSPSPYSRRQR  
 SVSPYSRRRSSSYERSGSGRSPSPYGRRRSSSPFLSKRSLRSPLPSRKSMKSRSRSP  
 AYSRHSSSSHKKKRSSSRSRHSSI SPVRLPLNSSLGAELSRKKKERAAAAAAAKMDGKES  
 KGSPVFLPRKENSSVEAKDSGLESKKLPRSVKLEKSAPDTELNVNTHLNTVEKNSSDTGK  
 VKLDENSEKHLVKDLKAQGTRDSKPIALKEEIVTPKETETSEKETPPPLPTIASPPPLP  
 TTTTPPPQTPPLPPLPPIPALPQQPPLPPSQPAFSQVPASSTSTLPPSTHSTSAVSSQAN  
 SQPPVQVSVKTQVSVTAAI PHLKTSTLPPPLPPLPPLPGGDDMDSPKETLPSKPVKKEKEQ  
 RTRHLLTDLPLPPELPGGDLSPDPSPEPKAITPPQQPYKKRPKICCPRYGERRQTESDWG  
 KRCVDKFDIIGIIGEGTYGQVYKARDKDTGELVALKKVRLDNEKEGFPITAI REIKILRQ  
 LIHRSVNMKEIVTDKQDALDFKKDKGAFYLVFEYMDHDLMLGLESGLVHFSEDHIKSPM  
 KQLMEGLEYCHKKNFLHRDIKCSNILLNNSGQIKLADFGLARLYNSEESRPYTNKVITLW  
 YRPPELLLGEERYTPAIDVWSCGICLGELFTKKPIFQANLELAQLELISRLCGSPCPAVW  
 PDVIKLPYFNTMKPKKQYRRRLREEFSFI PSAALDLDHMLTLDPSKRCTAEQTLQSDFL  
 KDVELSKMAPPDLPHWQDCHELWSKKRRRQSQSGVVVEEPPPSKTSRKETTSGTSTEPVK  
 NSSPAPPQAPAGKVESGAGDAIGLADITQQLNQSELAVLLNLLQSQTDL SIPQMAQLLNI  
 HSNPEMQQQLALNQSI SALTEATSQQQDSETMAPEESLKEAPSAPVILPSAEQMTLEAS  
 STPADMQNILAVLLSQLMKTQEPAGSLEENNSDKNSGPQGPRRTPTMPQEEAAACPPHIL  
 PPEKRPPEPPGPPPPPPPPPLVEGDLSSAPQELNPAVTAALLQLLSQPEAEPPGHLPHHEH  
 QALRPMEYSTRPRPNRTYGNTDGPETGFS AIDTDERNSGPALTESLVQTLVKNRTFSGSL  
 SHLGESSSYQGTGSVQFPGDQDLRFARVPLALHPVVGQPFLKAEGSSNSVVAETKLQNY  
 GELGPGTTGASSSGAGLHWGGPTQSSAYGKLYRGPTRVPPRGGRGRGVY

SEQ ID NO: 172\_AA789239\_H

MEMYETLGKVGESYGTVMKCKHKNTGQIVAIKIFYERPEQSVNKIAMREIKFLKQFHHE  
 NLVNLIEVFRQKKKIHLVFEFIDHTVLDELQHYCHGLESKRRLRKYLFQILRAIDYLHSNN  
 VIIHRDIKPENILVSQSGITKLCDFGFARTLAAPGDIYTDYVATRWYRAPELVVKDTSYG  
 KYVPVDI WALGCMIIEMATGNPYLPSSSDLDLLHKIVLVKXFMPELKAKLLQEAKVNSLI  
 KPKESSKENELRKDERKT VYTNLLSSSVLGKEIEKEKKPKEIKVRVIVKVGGRGDI SEP  
 KKKEYEGGLGQQDANENVHPMSPDTKLV TIEPPNPINPSTNCNGLKENPHCGGSVTMPPI  
 NLTNSNLMAANLSSNLFHPSVRLTERAKKRRTSSQSIGQVMPNSRQEDPGPIQSOMEKGI  
 FNERTGHSDQMANENKRKLNF SRSDRKEFHFPPELPVTIQSKDTKGMEVKQIKMLKRESKK  
 TESSKIPTLLNVDQNEKQEFIPLSLLSACCPIFTNICSQLTIRVEMAIARGRI

SEQ ID NO: 173\_AA124976\_M

LADIVHACLQIDPAERTSSTDLLRHDYFTRDGFIEKFIPELRAKLLQEAKVNSFIKPEN  
 FKENEPVRDEKKS VFTNTLLYGNPSLYGKEVDRDKRAKELKVRVIAKAGGKGDVPDQKKP  
 EYEGDHRQQGTADDTQPSLDDKKPSVLELTNPLNPSSENSDGVKEDPHAGGCMIMPPINLT  
 SSNLLAANLSSNLSHPNSRLTERTKKRRTSSQTIGQTLNSRQEDTGPTQVQTEKGAFNE  
 RTGQNDQISSGNKRKLNF PKCDRKEFHFPPELPFTVQAKEMKGMEVKQIKVLKRESKKTDS  
 SKIPTLLSMDPNQEKQEGGDGDCEGKNLKRNRFFFSR

SEQ ID NO: 174\_AA575635\_M CCRK\_M

SASGQLKIADFGLARVFS PDGGRLYTHQVATRWYRAPELLYGARQYDQGVDLWAVGCIMG  
 ELLNGSPLFP GENDIEQLCCVLRILGTSPSRVWPEITELPDYNKISFEEQAPVPLEEVLP  
 DASPQALDLLGQFLLYPPRQRIAASQALLHQYFFTA PLPAHPSELPIPQRPGGPAPKAHP  
 GPPHVHDFHVD RPIEESLLNPELIRPFIPEG

## FIGURE IN

SEQ ID NO: 175\_AA631990\_H

MIT SISTEKSGH THY PFMITTLQYYRGRGGKTAVVRHFS AEGPFAFAEMRHSKRTHCPDW  
DSRESWGHE SYRGSHKRKRSHSSTQENRHCKPHHQFKESDCHYLEARSLNERDYRDRRY  
VDEYRNDYCEGYVPRHYHRDIESGYRIHCSKSSVRSRRSSPKRKRNRHCS SHQSR SXEIV  
DTLGE GAFGKVVECIDHGMDGMHVAVKIVKNVGRYREAAARSEIQVLEHLNSTDPNSVFR C  
VQMLEWFDHHGHVCIVFELLGLSTYDFIKENSFLPFQIDHIRQMAYQICQSINFLHHNKL  
THTDLKPENILFVKSDYVVKYNSKMKRDERTLKNTDIKVVD FGSATYDDEHHSTLVSTRH  
YRAPEVILALGWSQPCDVWSIGCILIEYYLGFTVFQTHDSKEHLAMMERILGPI PQHMIQ  
KTRKRKYFHHNQLDWDEHSSAGRYVRRRCKPLKEFMLCHDEEHEKLF DLVRRMLEYDPTQ  
RITLDEALQHPFFD LLLKKK

SEQ ID NO: 176\_AA557536\_H

MCTVVDPRIVRRYLLRRQLGQGRTFREITLLQVSGLGPPVQSPCPGTDLSRQERNWPSWA  
PEHSPSWPSSRLRLSPQEFGDHPNIIISLLDVIRAENDRDIYLVFEFMDTDLNAVIRKGG L  
LQDVHVR SIFYQLLRATRFLHSGHVVRDQKPSNVLLDANCTVKLCDFGLARSLGDLPEG  
PEDQAVTEYVATRWYRAPEVLLSSHRYTASCPRYTLGVDMWSLGCILGEMLRGRPLFPGT  
STLHQLELILETIPPPSEEXRPRQTL DALLPPDTSPEALDLLRLLVFAPDKRLSATQAL  
QHPYVQRFHCPSDEWAREADV RPRAHEGVQLSVPEYRSRVYQMI LECGGSSGTSREKGPE  
GVSPSQAHLHKPRADPQLPSRTPVQGP RP RPQSSPGHDP AEHES PRAAKNVPRQNSAPLL  
QTALLNGERPPGAKEAPPLTSLSVKPSGRGAAPSLTSQAAAQVANQALIRGDWNRGGGV  
RVASVQQVPPRLPPEARPGRRMFSTSALQGAQGGARALLGGYSQAYGTVCHSALGHLPLL  
EGHHV

SEQ ID NO: 177\_N28606\_H, MOK\_H

MKNYKAIGKIGEGTFSEVMKMQSLRDGNYYACKQMKQRFESIEQVNNLREIQALRRRLNPH  
PNILMLHEVV FDRKSGSLALICELMDMNIYELIRGRRYPLSEKKIMHYMYQLCKSLDHIH  
RNGIFHRDV KPENILIKQDVLKLGDFGSCRSVYSKQPYTEYI STRWYRAPECLLT DGFYT  
YKMDLWSAGCVFYEIASLQPLFPGVNELDQISKIHDVIGTPAQKILT KFKQSRAMNFDFF  
FKKSGSIPLLTTNLS PQCLSLLHAMVAYDPDERIAAHQALQHPYFQEQRKTEKRALGSHR  
KAGFP EHPVAPEPLSNSCQISKEGRKQKQSLKQEEDRPKRRGPAYVMELPKLKLSGVVRL  
SSYSSPTLQSVLGS GTNGRVPVLRPLKCI PASKKTD PQKDLKPAPQQCRLPTIVRKGG R

SEQ ID NO: 178\_AB023153\_H, ICK\_H

MNRYTTIRQLGDGT YGSVLLGRSIESGELIAIKMKRKFYSWEECMNQREVKSLKKLNHA  
NVVKLKEVIRENDHLYFIFEYMKENLYQLIKERNKLPESAIRNIMYQILQGLAFIHKLG  
FFHRDLKPENLLCMGPELVK IADFG LAREIRSKPPYTDYVSTRWYRAPEVLLRSTNYSSP  
IDVWAVGCIMAEVYTLRPLFPGASEIDTIFKICQVLGTPKKT DWPEGYQLSSAMNFRWPQ  
CVPNNLKT LIPNASSEAVQLLRDMLQWDPKKRPTASQALRYPYFQVGHPLGSTTQNLQDS  
EKPQKGILERAGPPPYIKPVPPAQPPAKPHTRISSRQH QASQPPLHLTPYKAEVSRTDH  
PSHLQEDKPSLLFP SLHNKHPQSKITAGLEHKNGEIKPKSRRRWGLISRSTKSDDDWAD  
LDDLD FSPSLSRIDLKNKKRQSDDTLCRFESVLDLKPSEPVG TGNSAPTQTSYQRDTP T  
LRSAAKQHYLKH SRYLPGISIRNGILSNPGKEFIPPNPWSSSGLSGKSSGTMSVISKVNS  
VGSSSTSSSGLTGNYVPSFLKKEIGSAMQRVHLAPIPDPSPGYSSLKAMRPHPGRPFLDT  
QPRSTPGLIPRPPAAQPVHGRTDWASKYPSRR

SEQ ID NO: 179\_AA839940\_M

SSNNGGMSAEEEIGPGAEPMRGPSLATRDWRDET VGT TDLQQGIDPGAVSPEPGKD HAAQ  
GPGRTEAGRVSSAAEAAIVVLDDSAAPPAPFEHRVVS IKDTLISAGYTVSQHEVLGGGRF  
GOVHRCTERSTGLALAAKIIKVKNVKDREDVKNEVNIMNQLSHVNLIQLYDAFESKNSFT  
LIMEYVDGGELFD RITDEKYHLTEL DVVLFTRQICEGVHYLHQHYILHLDLKPENILCVS

## FIGURE 10

QTGHQIKI IDFG LARRYKPREKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVGVITYMLL  
SGLSPFLGETDAETMNFIVNCSWDFDADTFKGLSEEAKDFVSRLLVKEKSCRMSATQCLK  
HEWLNHLPAKASGSNVRLRSQQLLOKYMAQSKWKKH FHVVA AVNRLRKFP TCF

SEQ ID NO: 180\_AA460132\_H

MAAARATTPADGEEPAPAEALAAARERSSRFLSGLELVKQGAEARVFRGRFOGRAAVIK  
HRFPKGYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFFVDYASNCLYMEEIEGSV  
TVRDYIQSTMETEKTPOGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV  
LIDFGLSFISALPEDKGVLDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD  
EVRLRGRKRSMVG

SEQ ID NO: 181\_SGK034\_H

QREKVNQGNMPLQSTFLAMDTEEGVEVVWNEHFGDRKAFAAHEEKIQTVFEQLVLVDH  
PNIVKLHKYWLDTSEACARVIFITEYVSSGSLKQFLKKTCKNHKAMNARAWKRWCTQILS  
ALSFLHACSPPIIHGNLTSDTIFIQHNGLIKIGSVWHRIFSNALPDDLRSPIRAEREELR  
NLHFFPPPEYGEVADGTAVDIFSFGMCALEMAVLEIQTNQDTRVTEEAIAARARHSLSDPNM  
REFILCCLARDPARRPSAHSLLFHRVLFVHSLKLLAAHCFIQHQYLMPENNVVEEKTAM  
DLHAVLAELPRPRRPPLQWRYSEVSFMELDKFLEDVRNGIYPLMNFAATRPLGLPRVLAP  
PPEEVQAKTPTPEPFDSETRKVIQMQCNLSEDKARWHLTLLLVLLEDRLHRQLTYDLL  
PTDSAQDLASELVHYGFLHEDDRMKLAAFLESTFLKYRGTA

SEQ ID NO: 182\_AA103218\_M SGK034\_M

HASAPEYGEVNDGTGFVDIFSFGMCALEMAVLEIQANGDTRVTEEAIAARARHSLSDPNMR  
EFILSCLARDPARRPSAHLNLLFHRVLFVHSLKLLAAHCFIQHQYLMPENNVVEEKTAM  
LHAVLAEMPQPHGPPMQWRYSEVSFLELDKFLEDVRNGIYPLMNFAAARPLGLPRVLAPP  
PEEAQKAKTPTPEPFDSETRKVVQMOCNLERSEDKARWHLTLLLVLLEDRLHRQLTYDLLP  
TDSAQDLAAELVHYGFLHEDDRTKLAAFLETTFLKYRGTA

SEQ ID NO: 183\_NEK7\_H, N34132\_H

MSGGAAEKQSSTPGSLFLSPPAPAPKNGSSSDSSVGEKLGAAAADAVTGRTEEYRRRRHT  
MDKDSRGAAATTTTTEHRFFRRSVICDSNATALELPGLPLSLPQPSIPAAVPQSAPPEPH  
REETVTATATSQVAQQPPAAAAPGEQAVAGPAPSTVPSSTSKDRPVSQPSLVGSKEEPPP  
ARSGSGGSAKEPQEERSQQQDDIEELETKAVGMSNDGRFLKFDIEIGRGSFKTVYKGLD  
TETTVEVAWCELQDRKLT KSERQRFKEEAEMLKGLQHPNIVRFYDSWESTVKGKKCIVLV  
TELMTSGTLKTYLKRFKVMKIKVLRSWCRQILKGLQFLHTRTPLIHRDLKCDNIFITGP  
TGSVKIGDLGLATLKRASFASVIGTPEFMAPEMYEEKYDESVDVYAFGMCMLEMATSEY  
PYSECQNAAQIYRRVTSGVKPASFDKVAIPEVKEIEGCIQONKDERYSIKDLLNHAFQ  
EETGVRVELAEEDDGEKIAIKLWLRIEDIKKLKGYKDNEAIEFCFDLERDVPEDVAQEM  
VESGYVCEGDHKTMAKAIKDRVSLIKRKREQRQLVREEQENKKQEESLKKQVEQSSASQ  
TGIKQLPSASTGIPTASTTSASVSTQVEPEEPEADQHQQQLQYQQPSISVLSDGTVDSGGQ  
SSVFTESRVSSQQTVSYGFPXHEQAHTGTVPGHIPSTVQAQSOPHGVYPPSSVQQGIQQ  
TAPPQQTQYLSQSTSSSEATTAQPVSPQAPQVLPQVSAGKQSTQGVSVQVAPAEVAV  
AQPOATQPTTLASSVDSAHSDVASGMSDGNENVPSSSGRHEGRTTKRHYRKSVRSRSRHE  
KTSRPKLRILNVSNKGDRVVECQLETHNRKMVTFKFDLDGDNPEEIATIMVNNDFILAE  
RESFVDQVREIIEKADEMLSEDVSVEPEGDQGLSLOGKDDYGFSGSQKLEGEFKQPIPA  
SSMPQQIGIPTSSLTQVVHSAGRRFIVSPVPESRLRESKVFPSEITDTVAASTAQSPGMN  
LSHSASSLSLQQA FSELRRQMTEGPNTAPPNFSHTGPTFPVVPFLSSIAGVPTTAAAT  
APVPATSSPPNDISTSVIQSEVTVPTEEGIAGVATSTGVVTSGGLPIPPVSESPVLSSVV  
SSITIPAVVSISTTSPSLQVPTSTSEIVVSSTALYPSVTVSATSASAGGSTATPGPKPPA  
VVSQQAAGSTTVGATLTSVSTTTSPSTASQLSIQLSSSTSTPTLAETVVVSAHSLDKTS

## FIGURE 1P

HSSTTGLAFSLSAPSSSSSPGAGVSSYISQPGGLHPLVIPSVIASTFILPQAAGPTSTFL  
 LPQVPSIPPLVQPVANVIAVQQTLIHSQPCFALLPNQPHTHCPEVDSDTQPKAPGIDDIK  
 TLEEKLRSLFSEHSSSSGAQHASVSLETSLVIESTVTPGIPTTAVAPSKLLTSTTSTCLFP  
 TNLPLGTVALPVTPVVTPGQVSTPVSTTTSGVKPGTAPSKPPLTKAPVLPVGTETLPAGTL  
 PSEQLPFPFPGPSLTQSQCPLEDLDAQLRRTLSPEMITVTSAGVPVSMAPTAITEAGTQP  
 QKGVSVQKEGPVLATSSGAGVFKMGRFQVSVAADGAQKEGKNKSEDAKSVHFESSTSESS  
 VLSSSSPESTLVKPEPNGITIPGISSDVPESAHKTTASEAKSDTGQPTKVGRFQVTTTAN  
 KVGRFSVSKTEDKITDTKKEGPVASPPFMDLEQAVLPAVIPKKEKPELSEPSHLNGPSSD  
 PEAAFLSRDVEDDGGSGSPHSPHQLSSKSLPSQNLQSLSNSFNSSYMSSDNESDIEDDLK  
 LELRRLRDKHLKEIQDLQSRQKHEIESLYTKLGKVPPAVIIPPAAPLSGRRRRRPTKSKGS  
 KSSRSSSLGNKSPQLSGNLSGQSAASVLHPQQTLPHPGNIPESGQNQLLQPLKPSPPSSDN  
 LYSFTSDGAISVPSLSAPGQGNKATIIVQKQ

SEQ ID NO: 184\_BCON3\_H

MSEGESQTVLSSGSDPKVESSSSAPGLTSVSPVPTSTTSAASPEEEEESEDESEILEESP  
 CGRWQKRREEVNQRNVPGIDSAYLAMDTEEGVEVVWNEVQFSEKKNYKLQEEKVRAVFDN  
 LIQLEHLNIVKFHKYWADIKENKARVIFITEYMSSGSLKQFLKKTCKNHKTMNEKAWKRW  
 CTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIKIGSVAPDTINNHNKTCREEQKNL  
 HFFAPEYGEVTNVTAVDIYSFGMCALEMAVLEIQGNCESSYVPQEAISSAIQLLEDPLQ  
 REFIQKCLQSEPARRPTARELLFHPALFEVPSLKLLAAHCIVGHQHMI PENALEEITKNM  
 DTSAVLAEIPAGPGREPVTLYSQSPALEDKFLLEDVRNGIYPLTAFGLPRPQQPQQEEV  
 TSPVVPSPVKTPTPEPAEVETRKVVLMOCNIESVEEGVKHHLTLLLKLEDKLNRLHSCDL  
 MPNENIPELAAELVQLGFISEADQSRLTSLLEETLNKFNFNARNSTLNSAAVTVSS

SEQ ID NO: 185\_AA711829\_M

LKQFLKKTCKNHKTMNEKAWKRWCTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIK  
 IGSVAPDTINNHNKTCREEQKNLHFFAPEYGEVTNVTAVDIYSFGMCALEMAVLEIQGN  
 GESSYVPQEAISSAIQLLEDLSLQREFIQKCLQSEPARRPTARELLFHPALFEVPSLKLLA  
 AHCIVGHQHMI PENALEEITKNMDTSAVLAEIPAGPGREPVTLYSQSPALEDKFLLEDV  
 RYNGIYPLTAFGLPRPQQPQQEEVTSPVVPSPVKTPTPEPAEVETRKVVLMOCNIESVEEG  
 VKHHLTLLLKLEDKLNRLHSCDLMPNESIPDLAAELVQLGFISEADQSRLTSLLEETLNK  
 FNFRNSTLNTATVTVSS

SEQ ID NO: 186\_AA099102\_H

MSSCVSSQPSSNRAAPQDELGGRGSSSSSESQKPCEALRGLSSLSIHLGMESFIVVTECEP  
 GCAVDLGLARDRPLEADGQEVPLDTSGSQARPHLSGRKLSLQERSQGGLAAGGSLDMNGR  
 CICPSLPYSPVSSPQSSPRLPRRPTVESHHVSI TGMQDCVQLNQYTLKDEIGKGSYGVVK  
 LAYNENDNTYYAMKVLSSKKLIRQAAPRRPPPRGTRPAPGGCIQPRGPPIEQVYQEIAIL  
 KKLDHPNVVKLVVLDLDPNEDHLYMVFEVLNQGPVMEVPTLKPLSEDQARFYFQDLIKGI  
 EYLHYQKIIHRDIKPSNLLVGEDGHIKIADFGVSNEFKGSDALLSNYVGTAFMAPESLS  
 ETRKIFSGKAKDVWAMGVTLVCFVFGQCPFMDERIMCLHSKIKSQALEFPDQPDIAEDLK  
 DLITRMLDKNPESRIVVPEIKLHPWVTRHGAEPPLSEDENCTLVEVTEEEVENSVKHIPS  
 LATVILVKTMIKRKRSFGNPFEGSRREERSLSAPGNLLTKKPTRECESLSELKEARQRRQP  
 PGHRPAPRGGGGSALVRGSPCVESWAPAPGSPARMHPLRPEEAMEPE

SEQ ID NO: 187\_5R69\_17\_2\_H

MQEIPQEIQEIKKEQLSGSPWILLRENEVSTLYKGEYHRAPVAIKVFKKLQAGSIAIVR  
 QTFNKEIKTMKKFESPNI LRIFGICIDETVTPPQFSIVMEYCELGTRELLDREKDLTLG

## FIGURE 1Q

KRMVLVLGAARGLYRLHHSEAPELHGKIRSSNFLVTQGYQVKLAGFELRKTQTSMSLGT  
REKTDVRKSTAYLSPQELEDVFYQYDVKSEIYSFGIVLWEIATGDI PFQGEEDWLSQW  
L

SEQ ID NO: 188\_H85811\_H

MAPVYEGMASHVQVFSPTLQSSAFCSVKKLKIEPSSNWDMTGYGSHSKVYSQSKNIPLS  
QPATTTVSTSLPVPNPSPYPYEQTIVFPGSTGHIVVTSASSTSVTGQVLGGPHNLMRRSTV  
SLLDTYQKCGLKRKSEEIENTSSVQIIEEHPPMIQNNASGATVATATTSTATSKNSGSNS  
EGDYQLVQHEVLCMTNTYEVLEFLGRGTGQVVKCWKRGTNEIVAIIKILKNHPSYARQG  
QIEVSILARLSTESADDYNFVRAYECFQHKHNTCLVFEMLEQONLYDFLKQNKFSPLPLKY  
IRPVLQQVATALMKLKSGLIHADLKPENIMLVDPSPRQPYRVKVIDFGSASHVSKAVCST  
YLSRYRAPEIILGLPFCEAIDMWSLGCVIAELFLGWPLYPGDSEYDQIRYISQTQGLP  
AEYLLSAGTKTTRFFNRDTPSPYPLWRLKTPDDHEAETGIKSKEARKYIFNCLDDMAQVN  
MTTDLEGSMDLVEKADREFIDLLKMLTIDADKRITPIETLNHPFVTMTHLDDPHSTH  
VKSCFQNMIEICKRRVNMVDTVNQSKTPFITHVAPSTSTNLTMTFNNQLTTVHNQPSAASM  
AAVAQRSMPLQTGTAQICARPDPFQQALIVCPPGFQGLQASPSKHAGYSVRMENAVPIVT  
QAPGAQPLQIQPGLLAQQAQWPSGTQQIILLPPAWQQLTGVAHTSVQHATVI PETMAGTQQ  
LADWRNTHAHGSHYNPIMQQPALLTGHVTLPAAPLNVGVAVHVMRQOPTSTTSSRKSQKH  
QSSVRNVSTCEVSSSQAISSPQRSKRKVENTPPRCAMVHSSPACSTSVTCGWGDVASSTT  
RERQRQTIVIPDTPSPTVSVITISSDTDEEEEQKHAPTSTVSKQRKNVISCVTVHDSPTS  
DSSSNTSPYSVQQRAGHNNANAFDTKGSLENHCTGNPRTIIVPPLKTQASEVLVECDSLV  
PVNTSHHSSSYKSKSSSNVTSTSGHSSGSSSGAITRQQRPGPHFQQQQPLNLSQAQQHI  
TTDRTGSHRRQQAYITPTMAQAPYSFPHNSPSHGTVHPLHAAAAAAHLPTQPHLYTYTA  
PAALGSTGTVAHLVASQGSARHTVQHTAYPASIVHQPVPVSMGPRVLPSPTIHPSQYPAQF  
AHQTYISASPASTVYTGYPPLSPAKVNQYPYI

SEQ ID NO: 189\_DYRK3\_H

MMIDETKCPPCS NVLCNPSEPPPPRRLNMTAEQFTGDHTQHFLDGGEMKVEQLFQEFGR  
KSNTIQSDGISDSEKCSPTVSQGKSSDCLNTVKSNSSSSKAPKVPLTPEQALKQYKHHLT  
AYEKLIEIINYPEIYFVGPNAKKRHGVIGGPNNGGYDDADGAYIHVPRDLAYRYEVLKII  
GKGSFGQVARVYDHKLRYVALKMVRNEKRFHRQAEEIRILEHLKKQDKTGSMNVIHML  
ESFTFRNHVCMFELLSIDLIELIKKNKFQGFVSQVLRKFAQSILQSLDALHKNKIIHCD  
LKPENILLKHHGRSSTKVIDFGSSCFEYQKLYTYIQSRFYRAPEIILGSRYSTPIDISF  
RCILAEELLTGQPLFPGEDEGDQLACMMELLGMPPPKLLEQSKRAKYFINSKGI PRYCSVT  
TQADGRVVLVGGRSRRGKKRGPPGSKDWGTALKGCDYLFIEFLKRCLHWDPSARLTPAQ  
ALRHPWISKSVPRPLTTIDKVSGKRVVNPASAFQGLGSKLPPVVGIANKLKANLMSETNG  
SIPLCSVLPKLIS

SEQ ID NO: 190\_AA589241\_M DYRK3\_M

TRPELLGMPPQKLLEQSKRAKYFINSKGLPRYCSVSTQTDGRVVLGGRSRRGKKRGPPG  
SKDWATALKGCGDYLFIEFLKRCLQWDPSARLTPAQALRHPWISKSTPKPLTMDKVPGKR  
VVNPTNAFQGLGSKLPPVVGIA SKLKANLMSETSGSIPPLCSVLPKLIS

SEQ ID NO: 191\_5R72\_16\_2\_H

MAGGRGAPGRGRDEPPESYPQRQDHELQALEAIYGADFQDLRPDACGPVKEPPEINLVLY  
PQGLTGEEVYVKVDLRVKCPPTYPDVVPPEIELKNAKGLSNESVNLLKSRLEELAKKHCGE  
VMIFELAYHVQSFLSEHNKPPPKSFHEEMLERRAQEEQQRLLLEAKRKEEQEQREILHEIQ  
RRKEEIKKEKKRKEMAKQERLEIASLSNQDHTSKKDPGGHRTAAILHGGSPDFVNGKHF  
ANSSGRSRRERQYSVCNSEDSPGSCEILYFNMGSPDQLMVHKGKCIGSDEQLGKLVYNAL  
ETATGGFVLLYEWVLQWQKKMGPFLLTSQEKEKIDKCKKQIQGTETEFNSLVKLSHPNVVR

## FIGURE 1R

YLAMNLKEQDDSI VVDIILVEHISGVSLAAHLSHSGPI PVHQLRRYTAQLLSGLDYLSHSNS  
 VVHKVLSASNVLVDAEGTVKITDYSISKRLADICKEDVFEQTRVRFSDNALPYKTGKKGD  
 VWRGLGLLLLSLSQGECEYPTVTPSDLPADFQDFLKKCVCLDDKERWSPQQLLKHSFIN  
 PQPKMPLVEQSPEDSGGQDYVETVIPS NRLPSAAFFSETQRQFSRYFIEFEELQLLGKGA  
 FGAVIKVQNKLDGCCYAVKRIPINPASRQFRRIKGEVTLLSRLHHENIVRYNAWIERHE  
 RPAGPGTPPPDSGPLAKDDRAARGQPASDTDGLDSVEAAAPPPILSSSVIEWSTSGERSAS  
 ARFPATGPGSSDDEDDDEDEHGGVFSQSFLPASDES DIIFDNEDENSKSQNQDEDCNEK  
 NGCHESEPSVTTEAVHYLYIQMEYCEKSTLRDTIDQGLYRDTVRLWRLFREILDGLAYIH  
 EKGMIHRDLKPVNIFLDSDDHVKIGDFGLATDHLAFSADSKQDDQTGDLIKSDPSGHLTG  
 MVGTALYVSPVQGSTKSAYNQKVDLFSLGIIFFEMSYHPMVTASERIFVLNQLRDPSTP  
 KFPEDFDDGEHAKQKSVISWLLNHDPAKRPTATELLKSELLPPPMQEESELHEVLHHTLT  
 NVDGKAYRTMMAQIFSQRISPAIDYTYDSDILKGNFSIRTAKMQQHVCETIIRIFKRHGA  
 VQLCTPLLLPRNRQIYEHNEAALFMDHSGMLVMLPFDLRI PFARYVARNNILNLKRYCIE  
 RVFRPRKLDRFHPKELLECAFDIVTSTTNSFLPTAEIIYTIYEIIQEFPALQERNYSIYL  
 NHTMLLKAILLHCGIPEDKLSQVYIILYDAVTEKLTRREVEAKFCNLSLSSNSLCRLYKF  
 IEQKGDQLDLMPTINSLIKQKTGIAQLVKYGLKDL EEVVGLLKKLGIKLQVLINLGLVYK  
 VQQHNGIIFQFVAFIKRRQRAVPEILAAGGRYDLLIPQFRGPQALGPVPTAIGVSIADK  
 ISAAVLNMEESVTISSCDLLVSVGQMSMSRAINLTQKLWTAGITAEIMYDWSQSQEELQ  
 EYCRHHEITYVALVSDKEGSHVKVKSFEKERQTEKRVLETELVDHVLQKLRTKVTDERNG  
 REASDNLAVQNKGFSNASGLFEIHGATVVPDIVSVLAPEKLSASTRRRYETQVQTRLQT  
 SLANLHQKSSEIEILAVDLPKETILQFLSLEWDADEQAFNTTVKQLLSRLPKQRYLKLVC  
 DEIYNIKVEKKVSVLFLYSYRDDYYRILF

SEQ ID NO: 192\_R43524\_H, HRI\_H

MLGGNSGVRKREEEGDGAGAVAAPPAIDFPAEGPDPEYDESDVPAEIQVLKEPLQQPTFP  
 FAVANQLLLVSLLEHLSHVHEPNPLRSRQVFKLLCQTFIKMGLLSSTCSDEFSSLRLHH  
 NRAITHLMRSAKERVRQDPCEDISRIQKIRSREVALEAQT SRYLNEFEELVILGKGGYGR  
 VYKVRNKLDGQYYAIKKILIKGATKTVC MKVLREV KVLAGLQHPNIVGYHTAWIEHVHVI  
 QPRADRAAIELPSLEVLSDQEEDREQCGVKND ESSSSSIIFAEPTPEKEKRFGESDTENQ  
 NNKSVKYTTNLVIRESGELESTLELQENGLAGLSASSIVEQQPLPRNSHLEESFTSTEE  
 SSEENVNFLGQTEAQYHMLLHIQMQLCELSLWDWIVERNKRGREYVDESACPYVMANVAT  
 KIFQELVEGVFYIHNMGIVHRDLKPRNIFLHGPDQQVKIGDFGLACTDILQKNTDWTNRN  
 GKRTPTHTSRVGTCLYASPEQLEGSEYDAKSDMYSLGVVLELFPQFPFGTEMERAEVLTGL  
 RTGQLPESLRKRCPVQAKYIQHLTRRNSSQRPSAIQLLQSELFQNSGNVNLTLMQKII EQ  
 EKEIAELKKQLNLLSQDKGVRDDGKDDGGVG

SEQ ID NO: 193\_17000057519457\_H

MAAARATTPADGEEPAPAEALAAARERSRFLSGLELVKQGAEARVFRGRFQGRAAVIK  
 HRFPKGYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFFVDYASNCLYMEEIEGSV  
 TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV  
 LIDFGLSFISALPEDKGVDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD  
 EVRLRGRKRSMVG

SEQ ID NO: 194\_AA013524\_M

LVQQGAEARVFRGRFQGRAAVVKHRFPKSYRHPELEARLGRRRTVQEARALLRCRRAGIA  
 APVVFFVDYASNCLYMEEIEDSVTVRDYIQSTMETEKDPQCLLDLARRMGQVLAMHDQD  
 LIHGDLTTSNMLLRPLAQLHIVLIDFGLSFVSGLPEDKGVDLYVLEKAFLSTHPHTETA  
 FEAFKLSYGASSKSSPVLKKLDEVRLRGRKRSMVG



## FIGURE 1S

SEQ ID NO: 195\_17000139801197\_H, IRAKM\_H  
MAGNCGARGALSAHTLLFDLPPALLGELCAVLDS CDGALGWRGLAERLSSSWLDVRHIEK  
YVDQKGSGTRELLWSWAQKNKTIGDLLQVLQEMGHRRAIHLITNYGAVLSPSEKSYQEGG  
FPNILFKETANVTVDNVLIP EHNKGVLLKSSISFQNIIEGTRNFHKDFLIGEGEIFEVY  
RVEIQNLTYAVKLFKQEKMMQCKKHWRFLSELEVLLLFHHPNILELAAYFTETEFCL  
YPYMRNGTLFDR LQCVGDTAPLPWHIRIGILIGISKAIHYLHNVPSCSVICGSISSANIL  
LDDQFQPKLTDFAMAHFRSHLEHQ SCTINMTSSSSSKHLWYMPEEYIRQGKLSIKTDVYSF  
GIVIMEVLTGCRVVLDDPKHIQLRDLRELMEKRGLDSCLSFLDKKVP PCPRNFS AKLFC  
LAGRCAATR AKLRPSMDEV LNTLESTQASLYFAEDPPTSLKSFRCPSPLFLENVPSIPVE  
DDESQNNNLLPSDEGLRIDRMTQKTPFECSQSEVMFLSLDKKPESKRNEEACNMPSSSCE  
ESWFPKYIVPSQDLRPYKVNIDPSSEAPGHSCSRPVESSCSSKFSWDEYEYQYKKE

SEQ ID NO: 196\_AA840598\_M IRAKM\_M  
MWKRFLELEVLLFRHPHILELAAYFTETEKLC LVYPYMSNGTLFDR LQCTNGTTPLSW  
HVRISVLIGIAKAIQYLHNTQPCAVICGNVSSANILLDDQLQPKLTDFAAAHFRPNLEQQ  
SSTINMTGGGRKHLWYMPEEYIRQGR LSVKTDVYSFGIVIMEVLTGCKVVLDDPKHVQLR  
DLLMELMEKRGLDSCLSFLDRKIPPCPRNFS AKLFSLAGRCVATKAKLRPTMDEV LSSLE  
STQPSLYFAEDPPTSLKSFRCPSPLFLDNVPSIPVEDDENQNNH SVPPKEVLGTDRTQK  
TPFECSQSEVTFGLDRNRGNRGSEADCNVPSSSHEECWSP ELVAPSQDLSPTVISLGSS  
WEVPGHSYGSKPMEKRCSSGLFCSEHEQSKKQ

SEQ ID NO: 197\_AA088547\_H  
MASAVRGSRPWPRLGLQLQFAALLGLTSPQVHTLRPENLLL VSTLDGSLHALSKQTGDL  
KWTLRDDPVI EGPMYVTEMAFLSDPADGSLYILGTQKQQLMKLPFTIPELVHASPCRSS  
DGVFYTG RKQDAWFVVD PESGETQMTLTTEGPSTPRLYIGRTQYVTVMHDP RAPALRWNT  
TYRRYSAPPMDGSPGKYMSHLASCGMGLLLTVDPGSGTVLWTQDLGVPVMGVYTW HQDGL  
RQLPHLT LARDTLHFLALRWGHIRLPASGPRDTATL FSTLDTQLLMTLYVGKDETGFYVS  
KALVHTGVALVPRGLT LAPADGPTTDEVTLQVSGEREGSPSTAVRYPSGSVALPSQWLLI  
GHHELPPVLHTTMLRVHPTLGSGTAETRPENTQAPAFFLELLSLSREKLWDSELHP EEK  
TPDSYLG LGPQDLLAASLTAVLLGGWILFVMRQVVEKQQETPLAPADFAHISQDAQSLHS  
GASRRSQKRLQSPSKQAQPLDDPEAEQLTVVGKISFNPKDVLGRGAGGTFVFRGQFE GRA  
VAVKRLRLRECFLVRREVQLLQESDRHPNVLRYFCTERGPQFHYIALELCRASLQ EYVEN  
PDLDRGGLEPEVVLLQQLMSG LAHLHSLHIVHRDLKPGNILITGPDSQGLGRVVLSDFGLC  
KKLPAGRCFSLSHSGIPGTEGWMAPELLQLLPDSPTS AVDIFSAGCVFYVLSGGSHPF  
GDSLYRQANILTGAPCLAHLEEEVHDKVVARDLVGAMLSPLPQPRPSAPQVLAHPFFWSR  
AKQLQFFQDVSDWLEKESEQEPLVRALEAGGCAVVRDNWHEHIS MPLQTDLRKFRSYKGT  
SVRDLLRAVRNKKHHYREL PVEVRQALGQVPDGFVQYFTNRFPRLLLHTHRAMRSCASES  
LFLPYYPDSEARRPCPGATGR

SEQ ID NO: 198\_HGP\_6644466  
MEGISNFKTPSKLSEKKKSVLCSTPTINIPASPFMQKLGF GTGVNVYLMKRSPRGLSHSP  
WAVKKINPICNDHYRSVYQKRLMDEAKILKSLHHPNIVGYRAFTEANDGSLCLAMEYGG E  
KSLNDLIEERYKASQDPFPAAILKVALNMARG LKYLHQEKLLHGDIKSSNVVIKGD FE  
TIKICDVGVSLPLDENMTVTDPEACYIGTEPWKPKEAVEENGVI TDKADIFAFGLTLWEM  
MTLSIPHINLSNDDDDDEDKTFDESDFDDEAYYAALGTRPPINMEELDES YQKVIELFSVC  
TNEDPKDRPSAAHIVEALET DV

SEQ ID NO: 199\_AA449542\_M  
SPRGLSHSPWAVKKISLLCDDHYRTVYQKRLTDEAKILKNLNHPNIIGYRAFTEASDGSL  
CLAMEYGG EKSLNDLIEERNKDSGSPFPAAVILRVALHMARG LKYLHQEKLLHGDIKSS

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## FIGURE 1T

NVVIKGFETIKICDVGVSLPLDENMTVTDPEACYIGTEPWKPKEALEENGIITDFADV  
AFGLTLWEMMTLCIPHVNLPPDDVDDEATFDESDFDDEAYYAALGTRPSINMELDDSYQK  
AIELFCVCTNEDPKDRPSAAHIVEALELDGQCCGLSESKH

SEQ ID NO: 200\_5R57\_10\_2\_M TESK2\_M  
LLSDSLYLPWTVRVKLAYGIAVGLSYLHFKGIFHRDLTSKV

SEQ ID NO: 201\_AA232253\_H  
MSSLGASFVQIKFDDLQFFENC GGGSFGSVYRAKWISQDKEVAVKKLLKIEKEAEILSVL  
SHRNI IQFYGVILEPPNYGIVTEYASLGSLYDYINSNRSEEMDMDHIMTWATDVAKGMHY  
LHMEAPVKVIHRDLKSRNVVIAADGV LKICDFGASRFHNHTTHMSLVGTFPWWAPEVIQS  
LPVSETCDTYSYGVVLWEMLTREVFPKGLEGLQVAWLVEKNERLTI PSSCPRSFAELLH  
QCWEADAKKRPSFKQII SILESMSNDTSLPDKCNSFLHNKAWEWRCEIEATLERLKKLERD  
LSFKEQELKERERRLKMWEQKLTEQSNTPLLP SFEIGAWTEDDVYCWVQQQLVRKGDSSAE  
MSVYASL FKENNITGKRLLLLLEEDLDKMGIVSKGHI IHFKSAIEKLTHDYINLFHFPPL  
IKDSGGEPEENEKIVNLELVFGFHLKPGTGPQDCKWKMYMEMDGDEIAITYIKDVTFNT  
NLPDAEILKMTKPPFVMEKWIVGIAKSQTVECTVTYESDVRTPKSTKHVHLIQWSRTKPQ  
DEVKAVQLAIQTLFTNSDGNPGSRSDSSADCQWLDTLRMRQIASNTSLQRSQSNPILGSP  
FFSHFDGQDSYAAAVRRPQVPIKYQQITPVNQSRSSSPTQYGLTKNFSSLHLNSRDSGFS  
SGNTDTSSERGRYSDRSRNKYGRGSI SLNSSPRGRYSGKSQHSTPSRGRYPGKFYRVSQS  
ALNPHQSPDFKRSRDLHQPNTPGMPLHPETDSRASEEDSKVSEGGWTKVEYRKKPHRP  
SPAKTNKERARGDHRGWRNF

SEQ ID NO: 202\_AI375137\_H  
MGNYKSRPTQTCTDEWKKKVSESYVITIERLEDDLQIKEKELTEL RNIFGSDEAFSKVNL  
NYRTENGLSLLHLCCICGGKKSHIRTLMLKGLRPSRLTRNGFTALHLAVYKDNAELITSL  
LHSGADIQQVGYGGLTALHIATIAGHLEAADVLLQHGANVNIQDAVFFTPLHIAAAYGHE  
QVTRLLLLKFGADVNVSGEVD RPLHLASAKGFLNIAKLLMEEGSKADVNAQDNEDHVPLH  
FCSRFGHHDIVKYLLQSDLEVQPHVVNIYGDTPHLACYNKGFEVAKEIIQISGTESLTK  
ENIFSETAFHSACTYGKSIDL VKFLLDQNVININHQRDGTGLHSACYHGHIRLVQFLL  
DNGADMNLVACDPSRSSGEKDEQTCLMWAYEKGHDAIVTLLKHYKRPQDELPCNEYSQPG  
GDGSYVSVPSPLGKIKSMTKEKADILLRAGLP SHFHLQLSEIEFHEII GSGSFGKVYKG  
RCRNKIVAIKRYRANTYCSKSDVDMFCREVSILCQLNHPCV IQFVGACLN DPSQFAIVTQ  
YISGGSFLSLLHEQKRILD LQSKLIIA VDVAKGMEYLHNLTQPIIHRDLNSHNILLYEDG  
HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFSYALCLWEILT  
GEIPFAHLKPAAAAAD MAYHHIRPPIGYSIPKPISSLLIRGWNACPEGRPEFSEVVMKLE  
ECLCNIELMSPASSNSSGSLSPSSSSDCLVNRGGPGRSHVAALRSRFELEYALNARSYAA  
LSQSAGQYSSQGLSLEEMKRS LQYTPIDKYGYVSDPMSSMHFHSRNSSSFEDSS

SEQ ID NO: 203\_H97685\_H  
MESERSPLYRQLIDLGYLSSSHWNC GAPGQDTKAQSM LVEQSEKLRHLSTF SHQVLQTRL  
VDAAKALNLVHCHCLDIFINQAFDMQRDLQITPKRLEYTRKKENELYESLMNIANRKQEE  
MKDMIVETLNTMKEELLDDATNMEFKDVI VPENGE PVGTREIKCCIRQIQELIISRLNQA  
VANKLISSVDYLRESFVGT LERCLQSLEKSQDVSVHITSNYLKQILNAAHYHVEVTFHSGS  
SVTRMLWEQIKQIIQRITWVSPPAIT LEWK RKVAQEAIESLSASKLAKSICSQFRTRLNS  
SHEAFAASLRQLEAGHSGRLEKTEDLWLRVRKDHAPRLARLSLES RSLQDVLLHRKPKLG  
QELGRGQYGVVYLC DNWGGHFP CALKSVVPPDEKHWN DLAL EFHYMRSLPKHERLVDLHG  
SVIDYNYGGGSSIAVLLIMERLHRDLYTGLKAGLTLETRLQIALDVVEGIRFLHSQGLVH  
RDIKLNVL LDKQNRAKITDLGFC KPEAMMSGSI VGTPIHMAPELFTGKYDNSVDVYAFG

## FIGURE 1U

ILFWYICSGSVKLPEAFERCASKDHLWNNVRRGARPERLPVFDEECWQLMEACWDGDPLK  
RPLLGI VQ PMLQGIMNRLCKSNSEQPNRGLDDST

SEQ ID NO: 204\_W20810\_M  
DVNLKASKASDVYSFGILVWAVLAGREAEVLDKTSLIRETVCDRQSRPPLTELPPGSPET  
PGLEKLKELMIHCWGSQSENRP SFQDCEPKTNEVYNLVKDKVDAAVSEVKHYLSQHRSSG  
RNLSAREPSQRGTMDPCPRETMVSKMLDRHLLEEPSGPVPGKCPERQAQDTSVGPATPAR  
TSSDPVAGTPQIPHTLPFRGTTGPGVFTETPGPHQQRNQGDGRHGTPWYPWTPPNPMTGP  
PALVFNNCSEVQIGNYNLSLVAPPRTTASSSAKYDQAQFGRGRGWQPFHK

SEQ ID NO: 205\_AA744236\_H  
MGSENSALKSYTLREPPFTLPSGLAVYPVLQDGKFASV FVYKRENEDKVNKAAKHLKTL  
RHPCLLRFLSCTVEADGIHLVTERVQPLEVALETLSAEVCAGIYDILLALIFLHDRGHL  
THNNVCLSSVFVSEEDGHWKLGGMETVCKV SQATPEFLRSIQSIRDPASIPPEEMSPFTT  
LPECHGHARDAFSFGLTVESLLTILNEQVSADVLSSFQQLHSTLLNPIPKCRPALCTLL  
SHDFFRNDFLEVNF LKSLTLKSEEEKTEFFKFLDRV SCLSEELIASRLVPLLLNQLVF  
AEPVAVKSFLLPYLLGPKKDHAQGETPCLLSPALFQSRVIPVLLQLFEVHEEHVRMVLLSH  
IEAYVEHFTQEQLKKVILPQVLLGLRDTSDSIVAITLHSLAVLVSLLGPEVVVGERTKI  
FKRTAPSFTKNTDLSLEGDPFSQPIKFPINGLS DVKNTSEDSENFPSSSKKSEEWPDWSE  
PEEPENQTVNIQIWPREPCDDVKSQCTTLDVEESSWDDCEPSSLDTKVNPGGGITATKPV  
TSGEQKPIPALLSLTEESMPWKSSLPQKISLVQRGDDADQIEPPKVSSQERPLKVPSELG  
LGEEFTIQVKKKPKVDPEMDWFADMIPEIKPSAAFLILPELRTMVPKKDDVSPVMQFSS  
KFAAAEITEGEAEGWEEEGELNWEDNNW

SEQ ID NO: 206\_AI052250\_H  
MESMLNKLKSTVTKVTADVTSAVMGIPVTREFDVGRHIASGCNGLAWKIFNGTKKSTKQE  
VAVFVFDKKLIDKYQKFEKDQIIDSLKRGVQQLTRLRHPRLLT VQHPLEESRDCLAFCTE  
PVFASLANVLGNWENLPSPISPDIKDYKLYDVETKYGLLQVSEGLSFLHSSVKMVHGNIT  
PENIILNKSGAWKIMGDFCVSSTNPSEQEPKFPCKEWDPNLPSLCLPNPEYLAPEYILS  
VSCETASDMSYLGTVMYAVFNKGKPIFEVNKQDIYKSFSRQLDQLSRLGSSSLTNIPEEV  
REHVKLLLNVTPTVRPDADQMTKIPFFDDVGAVTLQYFDTL FQRDNLQKSQFFKGLPKVL  
PKLPKRIVIVQRILPCLTSEFVNPDMPVFLPNVLLIAEECTKEEYVKLILPELGPVFKQQ  
EPIQILLIFLQKMDLLLT KTPPDEIKNSVLPMVYRALEAPSIQIQELCLNIPTFANLID  
YPSMKNALIPRIKNACYKHLPLRFV

SEQ ID NO: 207\_AA278842\_H  
MWFFARDPVRDFPFELIPEPPEGGLPGPWALHRGRKKATGSPVSI FVYDVKPGAEEQTQV  
AKAAFKRFKTLRHPNILAYIDGLETEKCLHV VTEAVTPLGIYLKARVEAGGLKELEISWG  
LHQIVKALSFLVNDCSLIHNNVCM AAVFVDRAGEWKLGGLDYMYSAQGNGGGPPRKGIPE  
LEQYDPPELADSSGRVVREKWSADMWRLGCLIWEVFNGPLPRAAALRNPGKIPKTLVPHY  
CELVGANPKVRPNPARFLQNCRAPGGFMSNR FVETNLFLEEIQIKEPAEKQKFFQELSKS  
LDAFPEDFCRHKVLPQLLTAFEFGNAGAVVLTPLFKVGKFLSAEEYQQKIIPVVVKMFSS  
TDRAMRIRLLQQMEQFIQYLDEPTVNTQIFPHVHGF LDTNPAIREQTVKSMLLLAPKLN  
EANLNVELMKHFARLQAKDEQGPIRCNTTVCLGKIGSYLSASTRHRVLTSAFSRATRDPF  
APSRVAGVLGFAATHNLYSMNDCAQKILPVL CGLTVDPKSVRDQAFKAIRSFLSKLESV  
SEDPTQLEEVEKDVAASSPGMGAAASWAGAVTGVSSLT SKLIRSHPTTAPTETNIPQ  
RPTPEGVPAPAPTVPATPTTSGHWETQEEDKDTAEDSSTADRWDDEDWGSLEQEAESVL  
AQQDDWSTGGQVSRASQVNSDHKSSKSPESDWSSWEAEGSWEQGWQEPSSQEP PPDGTR  
LASEYNWGGPESSDKGDPFATLSARPSTQPRPDSWGEDNWEGLTDSRQVKAELARKKRE  
ERRREMEAKRAERKVAKGPMKLGARKLD

## FIGURE 1V

SEQ ID NO: 206\_AA599286\_H

MAFMKPPAGKVLDDTVPLTAAIEASQSLQSHTEYIIIRVQGGISVENSWQIVRRYSDFD  
LLNNSLQIAGLSLPLPPKKLIGNMDREFIAERQKGLQNYLNVITTNHILSNCELVKKFLD  
PNNYSANYTEIALQQVSMFFRSEPKWEVVEPLKDIGWRIRKKYFLMKIKNQPKERLVLSW  
ADLGPDKYLSDKDFQCLIKLLPSC LHPYIYRVTFATANESSALLIRMFNEKGTLKDLIYK  
AKPKDPFLKKYCNPKKIQGLELQQIKTYGRQILEVLKFLHDKGFPYGHLLHASNVMLDGD  
CRLLDLENSLLGLPSFYRSYFSQFRKINTLESVDVHCFGHLLYEMTYGRPPDSVPVDSFP  
PAPSMVAVVLESTLSCEACKNGMPTISRLLQMPLFSDVLLTTSEKPPQFKIPTKLKEALR  
IAKECIEKRLIEEQKQIHQHRRRLTRAQSHHGSEERKKRKILARKKSKRSALENSEEHSA  
KYSNSNNSAGSGASSPLTSPSSPTPPSTSGISALPPPPPPPPPPAAPLPPASTEAPAQLS  
SQAVNGMSRGALLSSIQNFOKGTLRKAKPVITVLRSSAEASCLHLEGKVLFYSSPLPPN  
YPLPGKVIAEPVQPQTVLFCRCSCCKQLFERNNSLSRIKLGWHAKKKKKK

SEQ ID NO: 209\_AA425725\_H

MSASTGGGGDSGGSGGSSSSSQASCGPESSGSELALATPVPQMLQGLLGSDDEEQEDPKD  
YCKGGYHPVKIGDVFNGRYHVVRKLGWGHFSTVWLCWDIQRKRFVALKVKSAGHYTETA  
VDEIKLLKCVRSDSPDPKRETIVQLIDDFRISGVNGVHVCMVLEVLGHQLLKWI IKS  
NYQGLPVPCVKSIVRQVLHGLDYLHTKCKI IHTDIKPENILLCVGDAYIRRLAAEATEWQQA  
GAPPPSRISIVSTAPQEVLTGKLSKNKRKKMRRKRKQKRLLEERLRDLQRLEAMEAATQA  
EDSGLRLDGGSGSTSSSGFSGSLFSPASCSILSGSSNQRETGGLLSPSTPFGASNLLVNP  
LEPQNADKIKIKIADLGNACWVHKHFTEDIQTRQYRAVEVLIGAEGPPADIWSTACMAF  
ELATGDYLFEPHSGEDYSRDEDHIAHIVELLGDI PPAFALSGRYSREFFNRRGELRHIHN  
LKHWGLYEVLMEKYEWPLEQATQFSAFLLPMMEYIPEKRASAADCLQHPWLN

SEQ ID NO: 210\_SGK022\_H

MEDFLLSNGYQLGKTIGEGTYSKVKEAFSKKHQKVAIKVIDKMGGPSEFIQRFLPRELQ  
IVRTL DHKNIIQVYEMLESADGKICLVMELAEGGDVFDVNLGGPLPESRAKALFRQMVE  
AIRYCHGCGVAHRDLKCENALLQG FNKLTDGFGAKVLPKSHRELSQTFCGSTAYAAPEV  
LQGI PHDSKKGDVWSMGVVLYVMLCASLPFDDTDIPKMLWQQQKGVSPFTHLSISADCQD  
LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 211\_AA060026\_M SGK022\_M

MEDFLLSNGYQLGKTIGEGTYSKVKEAFSKKHQKVAIKI IDKMGGPEEFIQRFLPRELQ  
IVRTL DHKNIIQVYEMLESADGKIYLMELAEGGDVFDVNLGGPLPESRAKALFRQMVE  
AIRYCHGCGVAHRDLKCENALLQG FNKLTDGFGAKVLPKSRRELSQTFCGSTAYAAPEV  
LQGI PHDSKKGDVWSMGVVLYVMLCASLPFDDTDIPKMLWQQQKGVSPFTHLGISTECQD  
LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 212\_AA399669\_H

MGKGDVLEAAPTTTAYHSLMDEYGYEVGKAIGHGSYGSVYEAFTKQKVMVAVKII SKKK  
ASDDYLNKFLPREIQVMKVL RHXYLINFYRAIESTSRVYII ELELAQGGDVLEWIQRYGA  
CSEPLAGKWFSQTLGLIAYLHKSIVHRDLKLENLLLDKWENVKISDFGFAKMVPSNQPV  
GCSPXYRQVNCFSHLSQTYCGSFAYACPEILRGLPYNPFLSDTWSMGVILYTLVVAHLPP  
DDTNLKKLLRETQKEVTFPANHTISQECKVQLLIACVAQWRKTQARPLSPLL

SEQ ID NO: 213\_AA758539\_H

MDDATVLRKKGYIVGINLGKGSYAKVKSAYSERLKFNVAVKIIDRRKTPTDFVERFLPRE  
MDILATVNHGSI IKTYEIFETSDGRIYIIMELGVQGDLLFEIKCQGALHEDVARKMFRQL  
SSAVKYCHDLDIVHRDLKCENLLLDKDFNIKLSDFGFSKRCLRDSNGRIILSKTFCGSA

## FIGURE 1W

YAAPEVLQSIPIYQPKVYDIWSLGVILYIMVCGSMPYDDSDIRKMLRIQKEHRVDFPRSKN  
LTCECKDLIYRMLQPDVSQRLHIDEILSHSWLQPPKPKATSSASFKEGEGKYRAECKLD  
TKTGLRPDHRPDHKLGAKTQHRLLVVPENENRMEDRLAETSRAKDHHS GAIEVGKAST

SEQ ID NO: 214\_AA883975\_H

MSGDKLLSELGYKLGRITIGESYSKVKVATSKKYKGTVAIKVVDRRRAPPDFVNKFLPRE  
LSILRGVRHPHIVHVFEFIEVCNGKLYIVMEAAATDLLQAVQRNGRIPGVQARDLFAQIA  
GAVRYLHDHHLVHRDLKCENVLLSPDERRVKLTDFGFGROAHGYPDLSTTYCGSAAAYASP  
EVLLGIPYDPKKYDVWSMGVVLYVMVTGCMFPDDSDIAGLPRRQKRGVLYPEGLELSERC  
KALIAELLQFSPSARPSAGQVARNCWLRAGDSG

SEQ ID NO: 215\_AA905446\_H

VGRQETGVRRWAFILCQPIISPPLTSSEFIQRFLPRELQIVRTL DHKNI IQVYEMLESADG  
KICLVMELAEAGDVDFDCVLNGGPLPESRAKALFRQMVEAIRYCHGCGVAHRDLKCENALL  
QGFNLKLTDFGFAKVLPKSHRELSQTFCGSTAYAAPEVLQGI PXKMLWQQQKGVSPFTHL  
SISADCQDLLKRLLPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 216\_H29974\_H

YSLLAIEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVELALAEFWALTSLKRRHQNV  
VQFEECVLQRNGLAQRM SHGNKSSQLYLRVETSLKGERILGYAEPCYLWFMFCEGG  
DLNQYVLSRRPDPATNKSFMLQLTSAIAFLHKNHIVHRDLKPDNILITERSGTPILKVAD  
FGLSKVCAGLAPRGKEGNQDNKNVNVN KYWLSSACGSDFYMAPEVWEGHYTAKADIFALG  
IIIWAMIERITFIDSETKKELLGTIYIKQGTEIVPVGEALLENPKMELHIPQKRRTSMSEG  
IKQLLKDMLAANPQDRPDFAFELETRMDQVTCAA

SEQ ID NO: 217\_AA498104\_M H29974\_M

PLLLPPPPAAMETGKENGARRGTS PERKRRSPVQORVLCEKLRPAAQAMPAGAEVPGEA  
FLARRRPDGGGGDVPARPRYSLLAEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVE  
LALAEFWALTSLKRRHQNVVQFEECVLQRNGLAQRM SHGNKNSQLYLRVETSLKGERIL  
GYAEPCYLWFMFMEYCEGGDLNQYVLSRRPDPATNKSFMLQLTSAIAFLHKNHIVHRDLK  
PDNILITERSGTPILKVADFGLSKVCAGLAPRGKEGNQDNKNVNVN KYWLSSACGSDFYM  
APEVWEGHYTAKADIFALGIIIWAMIERITFIDSETKKELLGTIYIKQGTEIVPVGEALLE  
NPKMELHIPQKRRTSMSEG VKQLLKDMLAANPQDRPDFAFELETRMDQVTCAA

SEQ ID NO: 218\_AA215311\_H

MVSSQPKYDLIREVGRGSYGVVYEAVIRKTSARVAVKKIRCHAPENVELALREFWALSSI  
KSQHPNVIHLEECILQKGMVQKMSHGNSSLYLQLVETSLKGEIAFDPRSAYYLWFMVD  
FCDGGDMNEYLLSRKPNRKTNTSFMLQLSSALAFHKNQIIHRDLKPDNILISQTRLDTS  
DLEPTLKVADFGLSKVCSASGQNPEEPVSVNKCFLSTACGTDFYMAPEVWEGHYTAKADI  
FALGIIIWAMLERITFIDTETKKELLGSYVKQGTEIVPVGEALLENPKMELLI PVKKKSM  
NGRMKQLIKEMLAANPQDRPDFAFELELRLVQIAFKDSSWET

SEQ ID NO: 219\_AA018361\_H

MRAAFPAGGAGGSVEPPSARPAPQAGTAARSEEAPARAQAAGMAGPGWGPPRLDGFILT  
ERLGS GTYATVYKAYAKKCTREVVAIKCVAKKSLNKASVENLLTEIEILKGIRHPHIVQL  
KDFQWSDNIYLIMEFCAGGDLRSFIHTRRILPEKVARVFMQQLASALQFLHERNISHLD  
LKPQNILLSSLEKPHLKLADFGFAQHMSPWDEKHVLRGSPLYMAPEMVCQRQYDARVDLW  
SMGVILYEALFGQPPFASRSFSELEEKIRSNRVIELPLRPLLSRDCRDLLQRLLERDPSR  
RISFQDFFAHPWVDLEHMPSGESLGRATALVVQAVKKDQEGDSAAALS LYCKALDFFVPA

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## FIGURE 1X

LHYEVDAQRKEAIKAKVGQYVSRAEELKAIVSSSNQALLRQGTSARDLLREMARDKPRLL  
AALEVASAAMAKEEAAGGEQDALDLYQHSLGELLLLLRSPRAGGGSCFTLRFRTSWPBLN  
T

SEQ ID NO: 220\_AA311714\_H

MENFILYEEIGRGSKTVVYKGRRKGTINFVAILCTDKCRRPEITNWVRLTREIKHKNIVT  
FHEWYETSNHLWLXENLPEDVVREFGIDLISGLHHLHKLGI LFCDISPRKILLEGPGTL  
KFSNFCCLAKVEGENLEEFFALVAAEEGGGDNGENVLKKSMSRVKGSVPYTAPEVVRGAD  
FSISSDLWSLGLLLEMFSGKPPFFSESVSELTEKILCEDPLPPIPKDSSRPKASSDFIN  
LLDGLLQRDPQKRLTWTRLLQHSFWKKAFAGADQESSVEDLSLSRNTMECSGPQDSKELL  
QNSQSRQAKGHKSGQPLGHSFRLENPTFEFRPKSTLEGQLNESMFLSSRPTPTSTAVEV  
SPGEDMTHCSPQKTSPLTKITSGHLSQODLESQMRELIYTDSDLVVTPIIDNPKIMKQPP  
VKFDAKILHLPTYSVDKLLFLKDQDWNDFLQQVCSQIDSTEKSMGASRAKLNLLCYLCVV  
AGHQEVATRLLHSPLFQLLIQHLRIAPNWDIRAKVAHVIGLLASHTTELQENTPVVETTS  
SIGIGILNCLVQHSTPVPRQCLVYV

SEQ ID NO: 221\_SGK384\_H

SLAHVLRARQILTEPEVRDYLRLGLVSGRLRYLHQRCILHR

SEQ ID NO: 222\_AA210451\_M SGK384\_M

MGQQHGTRNGLTHRELPRGVGLLLAMALMNVALYLCLDQLFISPGRSTADSRRCPPGYFR  
MGRMRNCSRWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALSRLTRLEMKEDFLH  
GLQMLKSLQSEHVVTLVGYCEEDGTILTEYHPLGSLSNLEETLNLSKYQDVNTWQHRLQL  
AMEYVSIINYLHHSPLGTRVMCDNDLPKTLQYLLTSNFSIVANDLDALPLVDHDSGVL  
IKCGHRELHGDFVAPEQLWPYGEDTPFQDDLMPSYNEKVDIWKIPDVSSFLLGHVEGSDM  
VRFHFLFDIHKACKSQIPAERPTAQNVLDAYQRVFHSRLRDTVMSQTKEML

PROTEIN NAME (OPTIONAL)

SEQ ID NO: 223\_SGK071\_2\_H

EVVAVQMMVECMDDHYASQALEELMPLLKLRAHISVYQELFITWNGEISSLYLCLVMEF  
NELSFQEVIEDKRKAKKIIDSEWMQNVLGQVLDALAYLHHLDI IHRNLKPSNII LISSDH  
CKLQDLSSNVLMTDKAKWNIRAEEDPFRKSWMAPEALNFSFSQKSDIWSLGCII LDMTSC  
SFMDGTEAMHLRKSRLRQSPGSLKAVLKTMEEKQIPDVETFRNLLPLMLQIDPSDRITIKD  
VVHITFLRGSFKSSCVSLTLHRQMVPASITDMLLEGNVASILGDAGDTKGERALKLLSMA  
LASYCLVPEGSLFMPLALLHMHQDLSCDQDRVPGKRDFASLGKLGKLLGPI PKGLPWPP  
ELVEVVVTMELHDRVLDVQLCACSLLLHLLGQALVHHPEAKAPCNQAITSTLLSALQSH  
PEEEPLLVMVYSLLAITTTQESSESLSEELQNAGLLEHILEHLNSSLERDVCASGLGLLW  
ALLLDDPILALQRPRKKRAPNHGKPKPKNPASTQSI IVNKAPLEKVPDLISQVLATYPA  
DGEMAEASCGVFWLLSLLGCIKEQQFEQVVALLLQSIRLCQDRALLVNNAYRGLASLVKV  
SELAAFKVVVQEEGGSGLSLIKETYQLHRDDPEVVENVGMLLVHLASYEEILPELVSSSM  
KALLQEIKERFTSSSLVSDSSAFSKPGLPPGGSPQLGCTTSGGLE

SEQ ID NO: 224\_AA118352\_M SGK071\_M

EEDPCQKSWMAPEALKFSFSTKS DIWSLGCII LD MATCSFLNDTEAMQLRKAIRHHPGSL  
KPILKTMEEKQIPGTDVYYLLL PFMLHINPSDR LAIKDVMQVTFMSNSFKSSSV ALNMQR  
QKVPIFITDVLLLEGNMANILGSWLCASFVNDSRHCDSGIGSQRLGFDQSVSWTEHPLKD  
VMQNFSSRPEVQLRAINKLLTMPEDQLGLPWPTELLEVISII KQHGRILDILLSTCSLL  
LRVLGQALAKDPEAEIPRSSLIISFLMDTLRSHPNSERLVNVVYNVLAIISSQGQISEEL  
EEEGFLQLAQENLEHFQEDRDICLSILSLLWSLLVDVVTVDKEPLEQLSGMVTWVLATHP  
EDVEIAEAGCAVLWLLSLLGCIKESQFEQVVLLLSIQLCPGRVLLVNNAFRGLASLAK

## FIGURE 1Y

VSELVAFRIVVLEEGSSGLHLIQDIYKLYKDDPEVVENLCMLLAHLTSYKEILPEMESGG  
IKDLVQVIRGRFTSSLELISYADEILQVLEANAQPGLOEDQLEPPAGQEAPLQGEPLFRP

SEQ ID NO: 225\_018653.9\_H

GRGRGAGHARGLGRGPAGRRAPPRSLSRPGPGPGSRAGPAGRGECSDAAPAGGSGRGFL  
RLLPAGLRPQALRSGSEPPRPGQSPEPSPAPGAGRRGGRGELARQIRARYEEVQRYSRG  
GPGPGAGRPERRRLMDLAPGGPGLPRPRPPWARPLSDGAPGWPPAPGPGSPGPGPRLGCA  
ALRNVSGAQYMGSGYTKAVYRVRLPGGAAVALKAVDFSGHDLGSCVREFGVRRGCYRLAA  
HKLLKEMVLLERLRHPNVLQLYGYCYQDSEIDPDTLTTITELGAPVEMIQLLQTSWEDRF  
RICLSLGRLLHHLAHSPLGSVTLDDFRPRQFVLVDGELKVTDLDDARVEETPCAGSTDCI  
LEFPARNFTLPCSAQGWCEGMNEKRNLYNAYRFFFTYLLPHSAPPSLRPLLDISIVNATGE  
LAWGVDETLAQLEKVLHLYRSGQYLQNSTASSSTEYQCI PDSTIPQEDYRCWPSYHHGSC  
LLSVFNLAEAVDVCESHAQCRAFVVTNQTWTGRQLVFFKTGWSQVVPDPNKTTYVKASG

SEQ ID NO: 226\_AA396601\_M

TRPGCAALRNVSGAQYVGSYTKAVYRVRLPGGAAVALKAVDFSGHDLGSCVREFGARRG  
CYRLAAHKLLKEMVLLERLRHPNVLQLYGYCYQDSEIDPDTLTTITELGAPVEMIQLLQTS  
SWEDRFRICLSLGRLLHHLAHSPLGSVTLDDFRPRQFVLVNGELKVTDLDDARVEETPCT  
SSADCTLEFPARNFTLPCSAQGWCEGMNEKRNLYNAYRFFFTYLLPHSAPPSLRPLLDISIV  
VNATGELAWGVDETLAQLETAHLFRSGQYLQNSTSSRAEYQRI PDSAITQEDYRCWPSY  
HHGGCLLSVFNLAEAIDVCESHAQCRAFVVTNQTWTGRKLVFFKTGWNQVVPDAGKTTY  
VKAPG

SEQ ID NO: 227\_VRK3\_H

MISFCPCGKSIQAAFKFCPYCGNSLPVEEHVGSQTFVNPVHVSFQGSKRGLNSSFETSP  
KKVKSSTVTSPRLSLFSDGDSSEEDTLSSSERSKSGSGSRPPTPKSSPQKTRKSPQVTR  
GSPQKTSCSPQKTRQSPQTLKRSRVTTSLALPTGTVLTDKSGRQWKLKSFQTRDNQGIL  
YEAAPTSTLTCDSGPQKQKFSCLKDAKDGRLFNEQNFFQRAAKPLQVKNWKKLYSTPLLA  
IPTCMGFGVHQDKYRFLVLP SLGRSLQSALDVSPKHVLSERSVLQVACRLDDALEFLHEN  
EYVHGNVTAENIFVDPEDQSQVTLGAGYGFAYRYCPSGKHVAYVEGSRSPHEGDLEFI SMD  
LHKGCGPSRRSDLQSLGYCMLKWLYGFLPWTNCLPNTEDIMKQKQKFVDKPGPFVGPCH  
WIRPSETLQKYLKVVMALTYEEKPPYAMLRNNLEALLQDLRVSPYDPIGLPMVP

SEQ ID NO: 228\_S71575\_M VRK3\_M

IPTCIGFGIHQDKYRFLVFP SLGRSLQSALDDNPKHVVSERCVLQVACRLDDALEYLHEN  
EYVHGNLTAENVFVN PEDLSQVTLVGYGFTYRYCPGGKHVAYKEGSRSPHDGDLEFI SMD  
LHKGCGPSRRSDLQTLGYCMLKWLYGSLPWTNCLPNTTEKITRQKQKYLDSPERLVGLCGR  
WNKASETLREYLKVVMALNYEEKPPYATLRNSLEALLQDMRVSPYDPLDLQMPV

SEQ ID NO: 229\_AA45427\_H

MGHALCVCSRGTVIIDNKRYLFIQKLGEFFSYVDLVEGLHDGHFYALKRILCHEQQDRE  
EAQREADMHRLFNHPNLRVAYCLRERGAKEAWLLLPFFKRGTWNEIERLKDKGNFL  
TEDQILWLLLGICRGLEAIAHAKGYAHRDLKPTNILLGDEGQPVLMDLGSMNQACIHVEGS  
RQALTLDQWAAQRCTISYRAPELFSVQSHCVIDERTDVWSLGCVLVYAMMFEGGPYDMVFQ  
KGDSVALAVQNQLSIPQSPRHSSALRQLLNSMMTVDPHQRPHIPLLLSQLEALQPPAPGQ  
HTTQI

SEQ ID NO: 230\_H05721\_H

MAVRQALGRGLQLGRALLRFTGKPGRAYGLGRPGPAAGCVRGERPGWAAGPGAEP RRVG  
LGLPNRLRFFRQSVAGLAARLQRQFVVRWGCAGPCGRAVFLAFGLGLGLIEEKQAESRR

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## FIGURE 1Z

AVSACQEIQAI FTQKSKFGPDPI DTRRLQGFRL EBYLIGQSIGKGCSAAVYEATMPTLP  
 NLEVTKSTGLLPGRGPFCT SAPGEGQERAPGAPAFPLAIKMMWNI SAGSSSEAILNTMSQE  
 LVPASRVALAGEYGAVTYRKS KRGPQLAPHPNI IRVLRAFTSSVPLLPGALVDYPDVLF  
 SRLHPEGLGHGRTLFLVMKNYPCTLRQYLCVNTPSPRLAAMMLLQ LLEGVDHLVQQGIAH  
 RDLKSDNILVELDPDGC PWLVIA DFGCCLADESIGLQLPFSSWYVDRGGNGCLMAPEVST  
 ARPGPRAVIDYSKADAWAVGAIAYEIFGLVNPFGYQGKAHLESRSYQEAQLPALPESVPP  
 DVRQLVRALLQREASKRPSARVAANVLHLSLWGEHILALKNLKLDKMGVWLLQQSAATLL  
 ANRLTEKCCVETKMKMLFLANLECETLCQAALLCSWRAAL

SEQ ID NO: 231\_AI086865\_H

MEKYERIRVVGRGAFGIVHLCLRKADQKLVI IKQIPVEQMTKEERQAAQNECQVLKLLNH  
 PNVEIYYENFLEDKALMIAMEYAPGGT LAEFIQKRCNSLLEEETILHFFVQIILLALHHVH  
 THLILHRDLKTQNILLDKHRMVVKIGDFGISKILSSKSTPCYISP ELCEGKPYNQKSDIW  
 ALGCVLYELASLKRAFEAANLPALVLKIMSGTFAPISDRYSPELRQLVLSLLSLEPAQRP  
 PLSHIMAQPLCIRALLNLHTDGREVRGPQQHREQDHQCPLQRG IIMTFGSGSNGCLGHGS  
 LTDISQPTIVEALLGYEMVQQVEEALSFTLLGSAPLDQEPLLSIDLGT AHSAAVTGEEDL  
 GSGDVNRLPSWERGHLLAGVASSTDVSTFSEGDCKEPKCCWRHKQCTGHI IYPFASDCV  
 RHSLHLHSVNHNCNSRLKDSSSEDSSSSRGAGPTCSHVIESPCFELTPEEEHVERFRYGW  
 CKSYRPVSVAVIHHPLYHECGADDLNXXKKRKR RRRRKS KPPIPTQVGPATASPD LGTSMAT  
 GTPDSTAPITITWRSESPTGKGQGSKVIKKVKKKKEKEKDKEEMDEKAKLKKKAKKGQLTK  
 KKSPVKLEPSPPDVSRSL SARQLARMSESSPESREELESEDSYNGRGQ GELSSEDIVESS  
 SPRKRENTVQAKKTGAKPSQARKVNKRKSPPGSNPNLS

SEQ ID NO: 232\_AA836348\_H

MSVLGEYERHCDSINSDFGSESGCGDSSPGPSASQGPRAGGGAAEQEELHYIPIRVLGR  
 GAFGEATLYRRTEDDSL VVWKEVDLTRLSEKERRDALNEIVILALLQHDNI IAYYNHFMD  
 NTTLLIELEYCNGGNLYDKILRQDKLFEEEMVWYLFQIVSAVSCIHKAGILHRDIKTL  
 NIFLTKANLIKLG DYGLAKKLNSEYSMAETLVGTPYMSPELCQGVKYNFKSDIWA VGCV  
 IFELLTLKRTFDATNPLNLCVKIVQGIRAMEVDSSQYSLELIQM VHSCLDQDPEQRPTAD  
 ELLDRPLLKR RRRSSTVTEAPIAVVTSRTSEVYVWGGGKSTPQKLDVIKSGCSARQVCAG  
 NTHFAVVTV EKELYTWVNMQGGTKLHGQLGHGDKASYRQPKHVEKLQ GKAI RQVSCGDDF  
 TVCVTDEGQLYAFGSDYYGCMGVDKVAGPEVLEPMQLNFFLSNPVEQVSCGDNHVVVLTR  
 NKEVYSWGCGEYGR LGLDSEEDYYTPQKVDVPKALIIVAVQCGCDGTFLLTQSGKVLACG  
 LNEFNKLGLNQCM SGIINHEAYHEVPYTTSFTLAKQLSFYKIRTIAPGKTHTA AIDERGR  
 LLTFGCNKCGQLGVGNYKKRLGINLLGGPLGGKQVIRVSCGDEFTIAATDEKVLNSKTIR  
 SNSSGLSIGTVFQSSSPGGGGGGGGGEEEDSQQESETPDPSGGFRGTMEADRGMEGLISP  
 TEAMGNSNGASSSCPGWLRKELENAEFIPMPDSPSPLSAAFSESEKDTLPYEELQGLKVA  
 SEAPLEHKPQVEASVTELF AFESQLVTSAESCSNLCWEGNTTDSSCVCVQLSAGGG

SEQ ID NO: 233\_R86668\_H, MKK6\_H

MNLLLSYRDVQDYSAI IELVETLQALPTCDVAEQHNVC FHYTFALNRRNRPGDRAKALSV  
 LLPLVQLEGSVAPDLYCMCGRIYKDMFFSSGFQDAGHREQAYH WYRKAFDVEPSLHSGIN  
 AAVLLIAAGQHFEDSKELRLIGMKLGCLLARKGCVEKMQYYWDVGFYLG AQIILANDPTQV  
 VLAAEQLYKLNAPIWYLV SVMETFLLYQHFRPTPEPPGGPPRAHFWLHFL LQSCQPFKT  
 ACAQGDQCLVLVLEMNKV LPAKLEVRGTD PVSTVTLSLLEPETQDI PSSWTFPVASICG  
 VSASKRDERCCFLYALPPAQDVQLCFPSVGH CQWFCGLIQAWVTNP DSTAPAEAEAGAGE  
 MLEFDYEYTETGERLVLGKGTYGVVYAGRDRHTRVRIAIKEI PERDSRFSQPLHEEIALH  
 RRLRHKNIVRYLGSASQGGYLKIFMEEVPGGSLSSLLRSVWG PLKDNESTISFYTRQILQ  
 GLGYLHDNHI VHRDIKGD NVLINTFSGLLKISDFGTSKRLAGITPCTETFTGT LQYMAPE  
 IIDQGPRGYGKAADIWSLGCTVIEMATGRPPFHELGS PQAAMFQVGMYKVHPPMPSSLSA



## FIGURE 1AA

EAQAFLLRTFEPDPRLRASAQTLLGDPFLQPGKRSRSPSSPRHAPRPSDAPSASPTPSAN  
STTQSQTFFPCPQAPSQHPPSPPKRCLSYGGTSQLRVPEEPAAEEPASPEESSGLSLLHQE  
SKRRAMLAAVLEQELPALAENLHQEQKQEQGARLGRNHVEELLRCLGAHIHTPNRRQLAQ  
ELRALQGRRLRAQGLGPALLHRPLFAFPDAVKQILRKRQIRPHWMFVLDSLLSRVRAALG  
VLGPEVEKEAVSPRSEELSNEGDSQQSPGQQSPLPVEPEQGPAPLMVQLSLLRAETDRLR  
EILAGKEREYQALVQORALQRLNEEARTYVLAPEPPTALSTDQGLVQWLQELNVDSTIQM  
LLNHSFTLHTLLTYATRDDLITYTRIRGGMVCRIWRILAQRAGSTPVTSGP

SEQ ID NO: 234\_PAK6\_H

MFGKKKKKIEISGPSNFEHRVHTGFDPPQEQKFTGLPQQWHSLLADTANRPKPMVDPSCIT  
PIQLAPMKTIVRGNKPKETSINGLLEDFDNISVTRSNSLRKESPTPDQGASSHGPCHA  
EENGFITFSQYSSSEDTTADYTTEKYREKSLYGDDLDPYRGSHAQKONGHVMKMKHGEA  
YYSEVKPLKSDFARFSADYHSHLDSLKSPSEYSDLKWEYQRASSSSPLDYSFQFTPSRTA  
GTSGCSKESLAYSESEWGPSLDDYDRPKSSYLNQTSPOPTMRQRSRSGSGLQEPMPFPG  
ASAFKTHPQGHSYNSYTYPRLSEPTMCIPKVDYDRAQMVLSPPLSGSDTYPRGPAKLPQS  
QSKSGYSSSSHQYPSGYHKATLYHHPSLQSSSQYISTASYLSSLSLSSSTYPSPSWGSSS  
DQQPSRVSHQFRAALQLVVSPPGDPREYLANFIKIGEGSTGIVCIATEKHTGKQVAVKKM  
DLRKQQRRELLFNEVVIMRDYHHDNVDMYSSYLVGDELWVMEFLEGGALTDIVTHTRM  
NEEQIATVCLSVLRALSYLHNQGVHRDIKSDSILLTSDGRIKLSDFGFCAQVSKEVPKR  
KSLVGTPYWMapevisRLPYGTEVDIWSLIGIMVIEMIDGEPPYFNEPPLQAMRRIRDSL  
PRVKDLHKVSSVLRGFLDLMLVREPSQRATAQELLGHPFLKLAGPPSCIVPLMRQYRHH

SEQ ID NO: 235\_SURTK106\_H

MNDRNEIQMEAKLQSLTIIAQEILCRFFITLRRHARFLLTKLGRQGMARSGITHSCAVCI  
LCGPSREGDSPVAMGMTRMLLECSLSDKLCVIEKQYEVIIIVPTLLVTIFLILLGVILWL  
FIREQRTQQQRSGPQGIAPVPPPRDLSWEAGHGGNVALPLKETSVENFLGATTPALAKLQ  
VPREQLSEVLEQICSGSCGPIFRANMNTGDPSPKPSVILKALKEPAGLHEVQDFLGRIQF  
HQYLKGKKNLVQLEGCCTEKLPLYMVLEDVAQGDLLGFLWTCRRDVMTMDGLLYDLTEKQ  
VYHIGKQVLLALEFLQEKHLFHGDVAARNILMQSDLTAKLCGLGLAYEVYTRGAISSTQT  
IPLKWLAPERLLLRLPASIRADVWSFGILLYEMVTLGAPPYPEVPPTSILEHLQRRKIMKR  
PSSCTHTMYSIMKSCWRWREADRPSPRELRLRLEAAIKTADDEAVLQVPELVVPELYAAV  
AGIRVESLFYNYSML

SEQ ID NO: 236\_AA098024\_M

LQEKHLFHGDVAARNILIQSDLTPKLCHLGLAYEVHAHGAISSARSSTIPLKWLAPERLL  
LRPASIRGDIWSFGILLYEMVTLGAPPYPEVPPTSILQYLQRRKIMKRPSSCSHAMYNIM  
KCCWRWSEDSRPLLQQLQRLEAASRSADDKAVLQVPELVVPELYADVAGIRAESISYSF  
SVL

SEQ ID NO: 237\_SGK2ALPHA\_H

MNSSPAGTPSPQPSRANGNINLGPSANPNAQPTDFDFLKVIGKGNYGKVLLAKRKSDGAF  
YAVKVLQKKSILKKKEQSHIMAERSVLLKNVRHPFLVGLRYSFQTPEKLYFVLDYVNGGE  
LFFHLQRERRFLEPRARFYAAEVASAIGYLHSLNIIYRDLKPENILLDCQGHVVLTDGFL  
CKEGVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSDVS  
QMYENILHQPLQIPGGRTVAACDLLQSLHKKDQQRQLGSKADFLEIKNHVFFSPINWDDL  
YHKRLTPPFNPNTGPADLKHFDPFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPE  
DDDILDC

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SEQ ID NO: 238 CCRK H

SEQ ID NO: 239 TSK2 H

MDRSKRNSIAGFP<sup>PR</sup>VERLEE<sup>F</sup>EGGGGGEGNV<sup>SQ</sup>VGRVWPSSYRALISAFSRLTRLDDFT  
CEKIGSGFFSEVFKVRHRASGQVMALKMNTLSSNRANMLKEVQLMNRLSHPNILRYINS  
NLEQLLDSNLHL<sup>PW</sup>TVRVK<sup>LAY</sup>DI<sup>AV</sup>GLSYLHFKGI<sup>FHR</sup>DLTSKNCLIKRDENGYS<sup>AV</sup>V  
DFGLAEKIPDVSMGSEKLAVVGS<sup>PFW</sup>MAPEVLRDEPYNEKADVFSYGIILCEIIARIQAD  
PDYLPRTENFGLDYDAFQHMVGDCPPDFLQLT<sup>FNC</sup>CCNMDPKLRPSFVEIGKTLEEILSRL  
QEEEQERDRKLQPTARGLLEKAPGVKRLSSLD<sup>DKI</sup>PHKSPCPRRTIWL<sup>SRS</sup>QSDIFSRKP  
PRTVSVLDPYYRPRDGAARTPKVNPFSARQDL<sup>MGG</sup>KIKFFDLPSKSVISLVFDLDAPGPG  
TMPLADWQEPLAPPIRR<sup>WRS</sup>LPGSP<sup>EFL</sup>HQEACPFVGREESLSDGPP<sup>PRL</sup>SSLKYRVKEI  
PPFRASALPAAQAHEAMDCSILQEENGFGSRPQGTSPCPAGASEEMEVEERPAGSTPATF  
STSGIGLOTQ<sup>GK</sup>QDG

## FIGURE 2A

SEQ ID NO: 1\_X69117\_H BARK2\_H

ATGGCGGACCTGGAGGCCGTGCTGGCCGATGTCAGTTACCTGATGGCCATGGAGAAGAGC  
AAGGCGACCCCGGCCCGCCGCGCCAGCAAGAGGATCGTCCTGCCGGAGCCAGTATCCGG  
AGTGTGATGCAGAAGTACCTTGCAGAGAGAAATGAAATAACCTTTGACAAGATTTTCAAT  
CAGAAAATTGGTTTCTTGCTATTTAAAGATTTTGTGTTGAATGAAATTAATGAAGCTGTA  
CCTCAGGTGAAGTTTTATGAAGAGATAAAGGAATATGAAAACTTGATAATGAGGAAGAC  
CGCCTTTGCAGAAGTCGACAAATTTATGATGCCTACATCATGAAGGAACCTTCTTCTCTGT  
TCACATCCTTTCTCAAAGCAAGCTGTAGAACACGTACAAAGTCATTTATCCAAGAAACAA  
GTGACATCAACTCTTTTTTCAGCCATACATAGAAGAAATTTGTGAAAGCCTTCGAGGTGAC  
ATTTTTCAAATTTTATGGAAAGTGACAAGTTCAGTAGATTTTGTGAGTGGAAAAACGTT  
GAATTAAATATCCATTTGACCATGAATGAGTTCAGTGTGCATAGGATTATTGGACGAGGA  
GGATTCGGGGAAGTTTATGGTTGCAGGAAAGCAGACACTGGAAAAATGTATGCAATGAAA  
TGCTTAGATAAGAAGAGGATCAAAATGAAACAAGGAGAAACATTAGCTTTAAATGAAAGA  
ATCATGTTGTCTCTTGTGTCAGCACAGGAGACTGTCCTTTCATTGTATGTATGACCTATGCC  
TTCCATACCCAGATAAACTCTGCTTCATCCTGGATCTGATGAACGGGGGCGATTTGCAC  
TACCACCTTTCAACAACCGGTGTGTTCTCTGAGAAGGAGATGCGGTTTTATGCCACTGAA  
ATCATTCTGGGTCTGGAACACGTGCACAATCGGTTTGTGTTGTCTACAGAGATTTGAAGCCA  
GCAAATATTCTCTTGATGAACATGGACACGCAAGAATATCAGATCTTGGTCTTGCTGCTGC  
GATTTTTCCAAAAAGAAGCCTCATGCGAGTGTGGCACCCTATGGGTACATGGCTCCCGAG  
GTGCTGCAGAAGGGGACGGCCTATGACAGCAGTGCCGACTGGTTCTCCCTGGGCTGCATG  
CTTTTCAAACCTTCTGAGAGGTACAGCCCTTTCAGACAACATAAAACCAAAGACAAGCAT  
GAAATTGACCGAATGACACTCACCGTGAATGTGGAACCTCCAGACACCTTCTCTCCTGAA  
CTGAAGTCCCTTTTGGAGGGCTTGCTTCAGCGAGACGTTAGCAAGCGGCTGGGCTGTCAC  
GGAGGCGGCTCACAGGAAGTAAAAGAGCACAGCTTTTTCAAAGGTGTTGACTGGCAGCAT  
GTCTACTTACAAAAGTACCCACCACCCTTGATTCCCTCCCCGGGGAGAAGTCAATGCTGCT  
GATGCCTTTGATATTGGCTCATTTGATGAAGAGGATACCAAAGGGATTAAGCTACTTGAT  
TGCGACCAAGAACTCTACAAGAACTTCCCTTTGGTTCATCTCTGAACGCTGGCAGCAAGAA  
GTAACGGAAACAGTTTATGAAGCAGTAAATGCAGACACAGATAAAATCGAGGCCAGGAAG  
AGAGCTAAAAATAAGCAACTTGGCCACGAAGAAGATTACGCTCTGGGGAAGGACTGTATT  
ATGCACGGGTACATGCTGAACTGGGAAACCCATTTCTGACTCAGTGGCAGCGTCGCTAT  
TTTTACCTCTTTCCAAATAGACTTGAATGGAGAGGAGAGGGAGAGTCCCGGCAAAATTTA  
CTGACAATGGAACAGATTCTCTCTGTGGAAGAACTCAAATTAAGACAAAAAATGCATT  
TTGTTTCAGAATAAAAGGAGGGGAAACAATTTGTCTTGCAATGTGAGAGTGATCCAGAGTTT  
GTGCAGTGGAAAGAAAGAGTTGAACGAAACCTTCAAGGAGGCCAGCGGCTATTGCGTCGT  
GCCCCGAAGTTCCTCAACAAACCTCGGTGAGTACTGTGGAGCTCCCAAAGCCATCCCTC  
TGTCACAGGAACAGCAACGGCCTCTGA

SEQ ID NO: 2\_AA144574\_M BARK2\_M

CTGCTTCGTAGTCTACAGAGACCTGAAGCCTGCGAACATCCTCCTAGATGAATATGGGCA  
CGTGAGGATATCGGATCTCGGCCTTGCTGTGATTTCTCCAAAAAGAAGCCTCATGCCAG  
CGTGGGCACCCATGGGTACATGGCTCCCGAGGTGTTGCAGAAGGGAACGTGCTATGACAG  
CAGCGCCGACTGGTTCTCCCTGGGCTGTATGCTCTTCAAACCTTCTGCGGGGCCACAGCCC  
CTTCAGGCAGCATAAAACCAAAGACAAGCATGAGATAGACCGAATGACCCTGACCGTGAA  
CGTGCAGCTTCCAGATGCCTTCTCCCCTGAGCTGAGGTCCCTCTTAGAGGGTTTGCTCCA  
GCGGGACGTGAGCCAGCGGCTGGGCTGCGGAGGAGGAGGGGCACGAGAGTTGAAGGAGCA  
CATCTTCTTCAAGGGCATTGACTGGCAGCATGTGTACTTACGGAAGTACCCGCCACCCCT  
AATCCCTCCTCGGGGAGAGGTCAACGCTGCAGATGCCTTCGATATCGGCTCCTTCGATGA  
GGAAGACACCAAAGGCATTAAGCTGTTGGACTGTGACCAGGACCTCTATAAGAACTTCCC  
ACTGGTGATCTCCGAGCGCTGGCAGCAAGAAGTGGTGGAGACCATCTATGACGCCGTCAA  
TGCTGATACTGATAAAATCGAGGCCAGGAAGAAGGCTAAAAATAAGCAACTTGGTCAAGA

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## FIGURE 2B

GSAAGATTACGCTATGGGSAAGGACTGCATCATGCACGGGTACATGCTGAAGCTGGGGAA  
CCCCCTTTCTCACACAGTGGCAAAGACGCTATTTTTACCTGTTCCCCAACAGACTGGAGTG  
GAGAGGAGAGGGGCGASTCTCGGCCAAAGTCTACTGACCATGGAACAGATCATGTCTGTGGA  
GGAGACCCAGATTAAAGACAGAAAGTGCATCTTACTCAGGATAAAGGGAGGGAAACAATT  
TGTCTTGCAATGTGAGAGTGACCCCGAGTTTGCACAGTGGCTGAAGGAGCTGACCTGCAC  
CTTCAATGAGGCCAGAGACTGCTGCGCCGTGCCCCCAAATTCCTCAACAAACCACGGGC  
CGCCATCCTGGAGTTCTCCAAGCCACCACTGTGTACAGAAATAGCAGCGGCCTCTGAAC  
CACAGAGCAGCGGGGCTGAAGGAGGGGCCCCAGCTCTTCAGCCCAGGAGTGGAACGAAG  
CCACGGGGAAACCGTGTGGGGCTAAGACACAGTGTCTTCTGAGCACTGACGGGGCTGCTCCA  
AGCCGAGGAGGCTCAGGACACCAGGGCGGCCTTCTGGGAGCTGGGACATCCTCGGGGCTG  
TCCTATCCACACTCGAAATTACTGAAGAAGCAGAGGCATTCTGCTGTG

SEQ ID NO: 3\_AA826850\_H

GAAGAGGATGGGCTCGTCCATGTGCGCGGCCACCGCGCGGAGGCCGGTGTGTTGACGACAA  
GGAGGACGTGAACTTCGACCACTTCCAGATCCTTCGGGCCATTGGGAAGGGCAGCTTTGG  
CAAGGTGTGCATTGTGCAGAAGCGGGACACGGAGAAGATGTACGCCATGAAGTACATGAA  
CAAGCAGCAGTGCATCGAGCGCGACGAGGTCCGCAACGTCTTCGGGGAGCTGGAGATCCT  
GCAGGAGATCGAGCACGTCTTCCTGGTGAACCTCTGGTACTCCTTCAGGACGAGGAGGA  
CATGTTTCATGGTCTGTGGACCTGCTACTGGGCGGGGACCTGCGCTACCACCTGCAGCAGAA  
CGTGCAGTTCTCCGAGGACACGGGTGAGGCTGTACATCTGCGAGATGGCACTGGCTCTGGA  
CTACCTGCGCGGCCAGCACATCATCCACAGAGATGTCAAGCCTGACAACATTCTCCTGGA  
TGAGAGAGGACATGCACACCTGACCGACTTCAACATTGCCACCATCATCAAGGACGGGGGA  
GCGGGCGACGGCATTAGCAGGCACCAAGCCGTACATGGCTCCGGAGATCTTCCAXTCTTT  
TGTC AACCGCGGGACCGGCTACTCCTTCGAGGTGGACTGGTGGTTCGGTGGGGGTGATGGC  
CTATGAGCTGCTGCGAGGATGGAGGCCCTATGACATCCACTCCAGCAACGCCGTGGAGTC  
CCTGGTGCAGCTGTTACGACCCGTGAGCGTCCAGTATGTCCCCACGTGGTCCAAGGAGAT  
GGTGGCCTTGCTGCGGAAGCTCCTCACTGTGAACCCCGAGCACCGGCTCTCCAGCCTCCA  
GGACGTGCAGGCAGCCCCGGCGCTGGCCGGCGTGCTGTGGGACCACCTGAGCGAGAAGAG  
GGTGGAGCCGGGCTTCGTGCCCAACAAAGGCCGTCTGCACTGCGACCCCACTTTGAGCT  
GGAGGAGATGATCCTGGAGTCCAGGCCCTGCACAAGAAGAAGAAGCGCCTGGCCAAGAA  
CAAGTCCCGGGACAACAGCAGGGACAGCTCCAGTCCGAGAATGACTATCTTCAAGACTG  
CCTCGATGCCATCCAGCAAGACTTCGTGATTTTTAACAGAGAAAAGCTGAAGAGGAGCCA  
GGACCTCCCGAGGGAGCCTCTCCCCGCCCTGAGTCCAGGGATGCTGCGGAGCCTGTGGA  
GGACGAGGCGGAACGCTCCGCCCTGCCCATGTGCGGCCCCATTTGCCCTCGGCCGGGAG  
CGGCTAGGCCGGGATGCCCGTGGTCTCACCCCTTGAGCTGCTTTGGAGACTCGGCTGCC  
AGAGGGAGGGCCATGGGCCGAGGCCTGGCATTACAGTTCCCAACCCAGCCTGGCTGGCGGT  
GCCACAGTGGCCCGGACACATTTACACCTCAGGCTCGTGGTGGTGCAGGGGACAAGAG  
GCTGTGGGTGCAGGGGACACCTGTGGAGGGCATTTCCCGTGGGCCCCCGAGACCCGCCTA  
GATGGAGGAAGCGCTGCTGGGCGCCCTCTTACCGCTCACGGGGAGCTGGGGCCATGGATG  
GGACAGGAGTCTTTGTCCCTGCTCAGCCCGGAGGCTGTGCACGGCCCTCGTCACAAGGTG  
ACCCTTGACGACAGGCCGCGGGTGGCCAGGCTCGGCTCAGTTCTTGAGGTCAGGGC  
ATGGGTGGGGTAGTGGGTGGGGAGGTGAATGTTTTCTAGAGATTCAAAGTCTCCAGCA  
ATTTCTGTATAGTTTTACCTCTGAGAATTACAATGTGAGAACCGCTC

SEQ ID NO: 4\_AA960957\_H

GTCCACATCCCGCATCCGGCATCCCAGCGGGCCGGGCATGTAGCAGCGGCAGCAACGGCG  
GAATATGGGCGGGAACCACTCCCAAGCCCCCGTGTTTGACGAGAATGAGGAAGTCAA  
CTTTGACCATTTTCAGATTCTGCGGGCCATTGGTAAAGGGAGTTTGGAAAGGTATGCAT  
CGTGCAGAAGCGAGACACTAAGAAAATGTATGCAATGAAGTACATGAACAAGCAGAAAGT  
CATCGAGAGGGATGAGGTTCCGAATGTTTTCCGGGAGCTGCAGATCATGCAAGGGCTGGA

## FIGURE 2C

GCACCCCTTCCTGGTCAATCTGTGGTACTCCTTCCAGGATGAGGAGGACATGTTTCATGGT  
GGTGGACCTGCTCCTGGGAGGCGACCTGCGCTACCATCTGCAGCAGAATGTGCATTTCAC  
AGAGGGGACTGTGAAACTCTACATCTGTGAGCTGGCACTGGCCCTGGAGTATCTTCAGAG  
GTACCACATCATCCACAGAGACATCAAGCCAGACAATATCCTGCTGGATGAACACGGACA  
TGTTTCACATTACAGACTTCAACATAGCGACGGTAGTGAAAGGAGCAGAAAGGGCTTCCTC  
CATGGCTGGCACCAAGCCCTACATGGCTCCAGAAGTATTCCAGGTGTACATGGACAGAGG  
CCCCGGATACTCGTACCCTGTGACTGGTGGTCCCTGGGCATCACAGCCTATGAGCTGCT  
GCGGGGCTGGAGGGCCGTACGAAATCCACTCGGTACGCCCATCGATGAAATCCTCAACAT  
GTTCAAGGTGGAGCGTGTCCACTACTCCTCCACGTGGTGCAAGGGGATGGTGGCCCTGCT  
GAGGAAGCTCCTGACCAAGGATCCTGAGAGCCGCGTGTCCAGCCTTCATGACATACAGAG  
CGTGGCCCTACTTGGCCGACATGAACTGGGACGCGGTGTTCAAGAAGGCACTGATGCCCCG  
CTTTGTGCCCCAATAAAGGGAGGTTGAACTGCGATCCACATTTGAGCTTGAAGAGATGAT  
TCTAGAATCCAAGCCACTTCACAAAAAGAAGAAGCGATTGGCAAAGAACAGATCCAGGGA  
TGGCACAAGGACAGCTGCCCGCTGAATGGACACCTGCAGCACTGTTTGGAGACTGTCCG  
GGAGGAATTCATCATATTCAACAGAGAGAAGCTCAGGAGGCAGCAGGGACAGGGCAGCCA  
GCTCTTGGACACCGACAGCCGAGGGGGAGGCCAGGCCCAAAGCAAGCTCCAGGACGGGTG  
CAACAACAACCTCCTCACCCACACCTGCACCCGTGGCTGCAGCAGCTGAGCCACACTTG  
TTGCTGCTCAACAGGACTGCACTCGTCTCTGCCCTGCCACCCAGAGCCCCCTCTTTGTGC  
CCTGATGGTCCCTGTCTCACCCCTGAAAACATCAGATGCAGAAAAAGCCCTGGACTTGGA  
GCTGGGAAGCCTGGGTTCTGGTCCCCTCTCCATGACTGATTCACGTGTGACCTCAGACAA  
GTCACGCCCTCTCTGTGCCTCCGTTTTCTGCATCTGCCAAAGGGGTAAACACTTCTGCC  
CCACTTCAAATTACAAGATTATGGGGAGAACCCAATTAGGTAGGAAACATGAAAAACCTT  
TGATATTTATAAAATCATTTTTTACGTGCAAAATATAACCTTAATATTTGAAGTGACCCCC  
ATTCCCCAAAGCAATCAAACCGTCATGACTTTGCAATTTGGCACATCCTAGCTTGTTAGA  
GGGCACTTCCGAAAAACACAGCCCTGACAGCAAAATAAAGGTCTGATATGTTGGCCCCCTT  
CTATGGAAACAACGCTGCCAAATCCTGGAGCAAAACCTGAAGTGTCTTCATGTGCATTCT  
CTGGCAGGCCACAGTCCTGAGCTTGTAAGATGGTGCAGCATGCAGACCAGACTTGTCCCC  
AAGGTCTCAGCGCTGCGGTCTCACTCCTCCCCCTCATTTAAGAAGACTATCCTTACCTTTT  
AGTTTCAGCAGTCCTCACCACCACCATATCCCCAGTGCTGGGATGGCACACAGGTGTCCA  
TTCAGATGAGAGTTGGGTCGCTGAGCATTGGTTACTCCTGCAGAGTGTAATCAGCACCCCC  
ATCCAACCTGGCCCGAAAGCCAGACCTGCAGCAGAACTCTCCAACCTCTCTATCAGCTTTC  
AGGGTTTTCTCTCCTGGGAAGGGTGTAAAATCAGCTTGTGAGATTCTTCTTACAGAGAGT  
ATCCAATCGGTATTGGTGGAGCGGCTCCCTATTTATACAATAGGAAGCATGGGTGCTTAG  
AAAGTTTATTTTCAGGAGGAAATGGGTTACACAAAAAGCAAACCTACATTCTGATCTGCT  
CAGGGAGAAGCTTGCCCTTGAACCTGGAAGATGTTGGGATGAGCAGGGAAAGCTTAGACTT  
TGGAGTCAGGTTTGTGTTTGAATCCAGCCCTGCTGGCTACTAACTAACTGGGAGACCTT  
AGGCAAAGCATGCAATCGCTCTGAATGGCAGTTTCCTCATTTTTTAAACAGGGATAATAAA  
ACTAATATTGCAGGGGAGTTACAGGGTTAAATAAGATCCTGTGTGTAACCCCAAGCATTG  
GATGACTCATAGAATGGCCTTTTTTGTGTCAGCATAATCGTCATCATTTATTAGATACTTTC  
TTCCTTCACTCACCCAGCAGGTCAGTTTTCTGTGCAAAACAAACCTGTTTAGGATTCTTCC  
AAATGTTCTTCTGGGGTCTTTGATATTTGTTTGTACATCCTGCTGAAGTTCGACTGTG  
TTTTTATTTTTTTCATCCAACCTTCCATTTTTTCACTTTTTTACATGATTACTCAATCCTTGGG  
GCTGTCCATGTGATCTCTTAGATTTCTTAAAAGACATTTTAATGTATGGTTAGGTTTTAT  
ATTTTTATTTTTTAAAAAAGAAATAGTCAGTGTTTTTCTCCTTTTCAACCGAGACTATTTT  
TGGATTGTGTGCTCCTCGTCAGTTGACTTGTTTTTGCACACTTTTCTTTACTTCATGTCCC  
CATCAACAACCGTCCTGCTCCCCACCTCCCCCAGGAAATAAGGGGCCTGCTCCTCTCCCT  
ACTGTGACCCTGGAGGCTCTTAAGATGATGATGGTTTTTTTTTATTGGGCTGAGTTCACGA  
ATTAGGGGCAGGAGCTGGAAGTCGCCCTAGGAACACCAGATTTCTGGTTCTGTTCAAGT  
TGGCATTTCTTGTGTTGGAATAAACTATTTCTTGGACATTCTTCT

## FIGURE 2D

SEQ ID NO: 5\_TBK1\_H

TCCTGAGTCTCGAGGAGGCCCGGGAGCCCCCGGGCGGTGGCGCGGGCGGAGACCCGGGCTG  
GTATAACAAGAGGATTGCTGATCCAGCCAAGATGCAGAGCACTTCTAATCATCTGTGGC  
TTTTATCTGATATTTTAGGCCAAGGAGCTACTGCAAATGCTTTTCGTGGAAGACATAAGA  
AAACTGGTGAATTTATTTGCTATCAAAGTATTTAATAACATAAGCTTCCTTCGTCCAGTGG  
ATGTTCAAATGAGAGAATTTGAAGTGTGAAAAAACTCAATCACAAAAATATTGTCAAAT  
TATTTGCTATTGAAGAGGAGACAACAACAAGACATAAAGTACTTATTATGGAATTTTGTG  
CATGTGGGAGTTTATACACTGTTTTAGAAGAACCTTCTAATGCCTATGGACTACCAGAAT  
CTGAATTCCTAATTGTTTTGCGAGATGTGGTGGGTGGAATGAATCATCTACGAGAGAATG  
GTATAGTGCACCGTGATATCAAGCCAGGAAATATCATGCGTGTTATAGGGGAAGATGGAC  
AGTCTGTGTACAACTCACAGATTTTGGTGCAGCTAGAGAATTAGAAGATGATGAGCAGT  
TTGTTTCTCTGTATGGCACAGAAGAATATTTGCACCCTGATATGTATGAGAGAGCAGTGC  
TAAGAAAAGATCATCAGAAGAAATATGGAGCAACAGTTGATCTTTGGAGCATTGGGGTAA  
CATTTTACCATGCAGCTACTGGATCACTGCCATTTAGACCCTTTGAAGGGCCTCGTAGGA  
ATAAAGAAGTGATGTATAAAATAATTACAGGAAAGCCTTCTGGTGCAATATCTGGAGTAC  
AGAAAGCAGAAAATGGACCAATTGACTGGAGTGGAGACATGCCTGTTTCTTGCACTCTTT  
CTCGGGGTCTTCAGGTTCTACTTACCCCTGTTCTTGCAAACATCCTTGAAGCAGATCAGG  
AAAAGTGTGGGGTTTTGACCAGTTTTTTTGAGAACTAGTGATATACTTCACCGAATGG  
TAATTCATGTTTTTTCGCTACAACAAATGACAGCTCATAAGATTTATATTCATAGCTATA  
ATACTGCTACTATATTTTCATGAAGTGTATATAAACAACCAAAATTTATTTCTTCAAATC  
AAGAACTTATCTACGAAGGGCGACGCTTAGTCTTAGAACCTGGAAGGCTGGCACAACATT  
TCCCTAAAACCTACTGAGGAAAACCTATATTTGTAGTAAGCCGGGAACCTCTGAATACCA  
TAGGATTAATATATGAAAAAATTTCCCTCCCTAAAGTACATCCACGTTATGATTTAGACG  
GGGATGCTAGCATGGCTAAGGCAATAACAGGGGTTGTGTGTTATGCCTGCAGAAATTGCCA  
GTACCTTACTGCTTTATCAGGAATTAATGCGAAAGGGGATACGATGGCTGATTGAATTAA  
TTAAAGATGATTACAATGAAACTGTTCAAAAAAGACAGAAGTTGTGATCACATTGGATT  
TCTGTATCAGAAACATTGAAAAAACTGTGAAAGTATATGAAAAGTTGATGAAGATCAACC  
TGGAAAGCGGCAGAGTTAGGTGAAATTTTCAGACATACACACCAAATTGTTGAGACTTTCCA  
GTTCTCAGGGAACAATAGAAACCAGTCTTCAGGATATCGACAGCAGATTATCTCCAGGTG  
GATCACTGGCAGACGCATGGGCACATCAAGAAGGCACTCATCCGAAAGACAGAAATGTAG  
AAAACTACAAGTCCTGTAAATTGCATGACAGAGATTTACTATCAGTTCAAAAAAGACA  
AAGCAGAACGTAGATTAGCTTATAATGAAGAACAATCCACAAATTTGATAAGCAAAAAC  
TGTATTACCATGCCACAAAAGCTATGACGCACTTTACAGATGAATGTGTTAAAAAGTATG  
AGGCATTTTTGAATAAGTCAGAAGAATGGATAAGAAAGATGCTTCATCTTAGGAAACAGT  
TATTATCGCTGACTAATCAGTGTTTTGATATTGAAGAAGAAGTATCAAAATATCAAGAAT  
ATACTAATGAGTTACAAGAACTCTGCCTCAGAAAATGTTTACAGCTTCCAGTGGAATCA  
AACATACCATGACCCCAATTTATCCAAGTTCTAACACATTAGTAGAAATGACTCTTGGA  
TGAAGAAATTAAGGAAGAGATGGAAGGGGTGGTTAAAGAACTTGCTGAAAATAACCACA  
TTTTAGAAAGGTTTGGCTCTTTAACCATGGATGGTGGCCTTCGCAACGTTGACTGTCTTT  
AGCTTTCTAATAGAAGTTTAAGAAAAGTTTCCGTTTGCACAAGAAAATAACGCTTGGGCA  
TTAAATGAATGCCTTTATAGATAGTCACTTGTTTCTACAATCCAGTATTTGATGTGGTGC  
TGTAATATGTACAATATTGTAAATACATAAAAAATATACAAATTTTTGGCTGCTGTGAA  
GATGTAATTTTATCTTTTAACATTTATAATTATATGAGGAAATTTGACCTCAGTGATCAC  
GAGAAGAAAGCCATGACCGACCAATATGTTGACATACTGATCCTCTACTCTGAGTGGGGC  
TAAATAAGTTATTTTCTCTGACCGCCTACTGGAAATATTTTTAAGTGGAACCAAAATAGG  
CATCCTTACAAATCAGGAAGACTGACTTGACACGTTTGTAATGGTAGAACGGTGGCTAC  
TGTGAGTGGGGAGCAGAACCGCACCACTGTTATACTGGGATAACAATTTTTTTGAGAAGG  
ATAAAGTGGCATTATTTTATTTTACAAGGTGCCCAGATCCCAGTTATCCTTGATCCATG  
TAATTCAGATGAATTATTAAGCAAACATTTTAAAGTGAATTCATTATTAAAAACATTTG  
ATTTTTTTCTTTTGGCCATAAATGTGTAATTGTCAATTAATTAAGGTCAATTTCAACT

## FIGURE 2E

GTTTTAAGCTGTATATTTCTTTAATTCTGCTTACTATTTTCATGGAAAAAATAAATTTCT  
CAATTTTAAAAAA

SEQ ID NO: 6\_AA305176\_H

TGGCTGCTCGCGGAGGGGCAGTGTACGCGGGGCGCTGTAGGCTGTCCAGCGATGGATCC  
CACCGCGGGAAGCAAGAAGGAGCCTGGAGGAGGCGCGGCGACTGAGGAGGGCGTGAATAG  
GATCGCAGTGCCAAAACCGCCCTCCATTGAGGAATTCAGCATAGTGAAGCCCATTAGCCG  
GGGCGCCTTCGGGAAAGTGTATCTGGGGCAGAAAGGCGGCAAATTGTATGCAGTAAAGGT  
TGTTAAAAAAGCAGACATGATCAACAAAAATATGACTCATCAGGTCCAAGCTGAGAGAGA  
TGCACTGGCACTAAGCAAAAGCCCATTCATTGTCCATTTGTATTATTCACTGCAGTCTGC  
AAACAATGTCTACTTGGTAATGGAATATCTTATTGGGGGAGATGTCAAGTCTCTCCTACA  
TATATATGGTTATTTTGATGAAGAGATGGCTGTGAAATATATTTCTGAAGTAGCACTGGC  
TCTAGACTACCTTCACAGACATGGAATCATCCACAGGGACTTGAAACCGGACAATATGCT  
TATTTCTAATGAGGGTCATATTAACTGACGGATTTTGGCCTTTCAAAAGTTACTTTGAA  
TAGAGATATTAATATGATGGATATCCTTACAACACCATCAATGGCAAAACCTAGACAAGA  
TTATTCAAGAACCCCAGGACAAGTGTATCGCTTATCAGCTCGTTGGGATTTAACACACC  
AATTGCAGAAAAAATCAAGACCCTGCAACATCCTTTCAGCCTGTCTGTCTGAAACATC  
ACAGCTTTTCTCAAGGACTCGTATGCCCTATGTCTGTAGATCAAAAGGACACTACGCCTTA  
TTCTAGCAAATTACTAAAATCATGTCTTGAAACAGTTGCCTCCAACCCAGGAATGCCTGT  
GAAGTGTCTAATTCTAATTTACTCCAGTCTAGGAAAAGGCTGGCCACATCCAGTGCCAG  
TAGTCAATCCACACCTTCATATCCAGTGTGGAATCAGAATGCCACAGCAGTCCCAAATG  
GGAAAAAGATTGCCAGGTTTGAGGGACATTTATCTTAATGAAAATCAATTATGTATGTCA  
AATGAATGTGAGAAATATTATACCTTTTCATATAAATTCATAAAGAAATGAAATTGTTA  
CATGAATGGCAGTCATAGTATTAATCAGAAATTCATTTTCCTGCACATTCTGTCAAATTC  
TTTTGAAATATTTTCAATTTCTCATTCAATTGTGACATTGTTCTTACTTGATTATATAATGA  
GATTCTTGCACTAAATTGATAATAAATGCTTGGCTTCTGTGTATCTAGGTGGACCTCACT  
TGTTTTTTAGAAGTCCTTCCCATGATACAGACATTGGCTTGTTGGTTTTGTTTTATTTTGT  
TTTTAACATATGTCATTTAAAACTCATATTACCTCCTTTT

SEQ ID NO: 7\_AA116841\_M

CCACGCGTCCGATCCCATGGCCAGAAGGCGAAGAAAGCTATCTGATAATGCTCAAAGTG  
CAATGGACATGCTTTTAACCATTTGATGATTCAAAGAGAGCTGGAATGAGAGAACTAAAC  
AGCATCCTCTCTTCAGTGAAGTGGACTGGGAAAATCTGCAGCATCAGACTATGCCTTTCG  
TACCCCAACCAGACGACGAAACAGATACATCTATTTTGAAGCCAGAAATAATGCTCAAC  
ATCTGACCGTATCTGGGTTTAGTCTGTAGCACATGCGTGTCAATTTTATCTAATTGTGA  
TATAGAATTAAGTTTTACAGTAATATGCTACTTAATACTAGATTGGTCTAAATGGGATAA  
AAGTCATTATTTTACCCAGACTGAACAGCTTTTAATTACTAAGTACAACAGTTTTTACAG  
AATTAATACTATAAGCAATATAATCAGTAATTAATCTTTACCTTAGAACTGTATATAA  
GCCATAATAGCTTTTTTTCATCTTATTTATTCACTGCACTTTATGAAGAGCAAAGTATCAA  
TAACTAAAACACTACCACTCTAAATAGAGGGAGTGAGCCGT

SEQ ID NO: 8\_AA256100\_H

AGGGAGCTGACGGGCGCCCGGCGGCTGCGGTCCGTGCGGAGGCTGAGCCGGCCGCGGGC  
GCGACCGGAGGCAGTTTCCGTTACTATGGCAATGACGGCAGGGACTACAACAACCTTTCC  
TATGAGCAACCATAACCGGGAAGAGTGACTGTAGCCAAGCTCACATTGGAGAATTTTAA  
TAGCAACCTAATTTTACAGCATGAAGAGAGAGAAACCAGGCAGAAGAAATTAGAAGTGGC  
CATGGAAGAAGAAGGATTAGCAGATGAAGAGAAAAAGTTACGTCGATCACAACACGCTCG  
CAAAGAAACAGAGTTCTTACGGCTCAAAGGACCAGACTTGGCTTGGATGACTTTGAGTC  
TCTGAAAGTTATAGGAAGAGGAGCTTTTGGAGAGGTGCGGTTGGTCCAGAAGAAAGATAC  
AGGCCATATCTATGCAATGAAGATATTGAGAAAGTCTGATATGCTTGAAAAAGAGCAGGT

FIGURE 2F

GGCCCATATCCGAGCAGAAAAGAGATATTTTGGTAGAAGCAGATGGTGCCTGGGTGGTGAA  
GATGTTTTACAGTTTTTCAGGATAAGAGGAATCTTTATCTAATCATGGAATTTCTCCCTGG  
AGGTGACATGATGACATTGCTAATGAAGAAAGACACCTTGACAGAAAGAGGAAACACAGTT  
CTACATTTTCAGAGACTGTTCTGGCAATAGATGCGATCCACCAGTTGGGTTCATCCATCG  
GGATATTAAGCCAGACAACCTTTTATTGATGCCAAGGGTCATGTAAAATTATCTGATTT  
TGGTTTTATGTACGGGATTAAAGAAAGCTCACAGGACTGAATTTTATAGAAATCTCACACA  
CAACCCACCAAGTGACTTCTCATTTTCAGAACATGAACTCAAAGAGGAAAGCAGAACTTG  
GAAGAAGAACAGGAGACAACCTGGCATATTCCACAGTTGGGACACCAGATTACATTGCTCC  
AGAAGTATTCATGCAGACTGGTTACAACAAATTGTGTGACTGGTGGTCTTTGGGAGTGAT  
TATGTATGAAATGCTAATAGGATATCCACCTTTCTGCTCTGAAACACCTCAAGAAACATA  
CAGAAAAGTGATGAACTGGAAAGAACTCTGGTATTTCTCCAGAGGTACCTATATCTGA  
GAAAGCCAAGGACTTAATTCTCAGATTTTGTATTGATTCTGAAAACAGAATTGGAAATAG  
TGGAGTAGAAGAAATAAAAGGTCATCCCTTTTTTTGAAGGTGTCGACTGGGAGCACATAAG  
GGAAAGGCCAGCAGCAATCCCTATAGAAATCAAAGCATTGATGATACTTCAAATTTTGA  
TGACTTCCCTGAATCTGATATTTTACAACCAGTGCCAAATACCACAGAACCGGACTACAA  
ATCCAAAGACTGGGTTTTTCTCAATTATACCTATAAAAGGTTTGAAGGGTTGACTCAACG  
TGGCTCTATCCCCACCTACATGAAAGCTGGGAAGTTATGAATGAAGATAACATTCACCCA  
TAACCAAGAGAACTCAGGTAGCTGCATCACCAGGCTTGCTTGGCGTAGATAACAATACAC  
TGAAATACTCCTGAAGATGGTGGTGCTTATTGACTACAAGAGGAAATTCTACAGGATTAG  
GATTTCTAAGACTACTATAGGAATTGGTTGGCAGTGCCAGCTGGCTCTTTTTTTTAATAT  
TTTATTATTTTTGTAACTTTATTATATGAAGGTACTGGAATAAAAGGAACAGACATCCC  
TTTCTAACTGCACTGCCTACATGCGTATTAAGGTCCATTCTGCCTGTGTGTGCTGTGGCT  
TTGAACTGTAACACCTCTAATCAATTCAGGAGAAACACATATCATTTAAAGCAACATAGG  
CTAACCTGTAGGTAACACTGCAGTATTGATGTTTTACTGCAAATCTTATGGGTCTAGATA  
ATCAGTAAAAGCCATCTTCCATAGTTGGTGTTAGAACATTGCCCTATTGGTTTGGACATC  
TGTAGAATATATATGAAGACAATTTCTGTAATGGTTTTAAGAGATTTAAAAAGAAATTCA  
CTGGTTCTTTACAAAATAGAATTTATCATCAAGTTATTACACAACTTCACAGTAAGGAG  
TGACAAGTTTTATAATAAGGAAGACAAAGTTTAACACCTTCACTCAAGCACTCCACTAATA  
TATTTACGTTGCATTACAGAAATACTGATGACCTTCATATACGTAGTCTGTATACTCATAG  
GGAGATGTACTGTATTATATAACATGTAAAGTTGATTTTCTTGTGACAAGAGAACTTCTT  
TTTTTAAACAAGAGGACATGGCATTATTTTAATTTGATTATGGTGAGFTGAATTTAAGACA  
TGACCATGAAGGCTGCTTGTAGAATTAGTGTATTTTTATTAACTATTTTTTTTAAATGTC  
AACTTCTATCATGTAAATGGACTTATAGAGAACA AAAAGCTATTTACTTTGGTTTTCTA  
GAAAGTTGTTACATATCATGGCTGGTTAACTTTTATTTCTTTTGATGAAAATTTTTCTCTT  
TGATAGTACTTGTATTATTGTGCCATTATTTTCTTATGCTCCAAATGTACCAAAGATCTT  
GAACAGAGTGGATGTTTCACAACTGAGTAGAATTTTCTTTCTGTGGGCATGCTGTATTTC  
AGACCTGACAGATCTTTGATAGAGGTCAGCTTATTAAAGGGCAATATTGTTCTTGTTTAG  
CTACATCACTGTGGTGAATATAGATGGAATTAAGGAAGTAAATGCAGGCCAGGGGGTTGT  
GATGAGAGGATAGGGGAGATAATATCAGCATCAAATTCTTTGGGTATCTCTCTAAGAATT  
AAATAATCTTTTCTAGCTTAATATTTTAAATTCTAATTCAAACAACCTCTGAGGTTTTGGTT  
TCATTAGTAATAGTTGAGGAATAATATACTAGCAAAGAATGGCCTAATGTTTGTCTATAAC  
TGTTAATGGATGAAATTTTTTAAAGATACAACCATGATAACCATTAATAATGATCTATGA  
TCAAAATCTAAAGTGATGAATTATTTGTAGGAATGTCTTCCTAATGGGGGAAGAATTGCAT  
AGGAGCATTATGCAAATCTACACAAGCTTTTATAAATGTTGCTGCTGGGTAGCTCCACAG  
TGTTTTCATAGGCCATCCTGTTTCCCCCAACTCCCCCATTTTTTGGTTTTGTTTCTTTTTAA  
ATATTTGTTGAGTACTTACGTGTTTATCTAACAGTTCACTTCCATTTTTCTAGTCTGGAT  
TTTTTGAGTATTTAGGAAAGAGAGCTATTA AAAACTCTGGGGATTTCTCAATGTGACTAA  
CTCTAATTTTTCTAATTATACTGCCTTTAATTAACATAATATTA ACTTTTGCTGAGGTT  
TATGAGATTTTCTCACCCACATCGCTCCCCTTTTTTTAAAGGACTGTTTTGCTAGTG  
TGATAATGAATAGGTAAGATATGAGATAATTGCAACATTGTCCTAGTTCTAGTATGGTAA



## FIGURE 2G

CTATTCTTGAAATGGTATTGAAAAATACCGTTAATTCAAATTGACAGAGATTGATAAAAA  
GAAACTGATTTACCTAAGTTTACTTTTTTAATTGCATAATAGAGCATTTTTTGTGTTTGTGAGT  
TCCCTCATTCTTATTACCAGAAAGAGCTTGCAAATAGTTTTACTTTCTTGGCACTGGAAG  
GGTAGTTCTGGAAAGCTACTTTGTTGAGAGTCTCATTCTTCCCTGGAGTTAATAGAGTGA  
TTCACAATCTTTGGGGTTTTCTCCTCATCAAAGCATTTCTTAAGTGCCTATCTAAAAGC  
AATTAAAGACTGTGTCTGCCCTTTAGAAGCTAAGAATTTGATTTCATGATGCAAATTA  
AGATAATTTGCAAAGTACCCTTGAGATTGAATTTTCTCTATTATATATTTCCCATATTTT  
AGGTGAATAATTTAATTTAAATGACAAAACCTATCTAGTCAACTGGGCATAATGACATT  
TTCTTTAAATTAGACTCTATTTTGAATTAAGAGTTTTATTATAAACCGTGTGTTTTTGT  
GTTTTTCTAAGTATATAGAAAGCTTGTATAATTCAGATTTATCAATTTCTGATTTAATG  
TAGACTTTGACTTTTTTTATTAATAAACCTTTGTATTAAAGCAAGTTATGTTATTTTTCTTT  
TATGCATTTATTACTAACATAGCTTTAAATCTTTAAATGTATTGAAGCATTGTGCTGTCT  
GAAAATAAGGAATTGCTTATAAACAGCCACTTCTGAATACAATATGTAGCTGATTTAAT  
AAGCTAGTTAGTGAATGGAAAATAAGTGTGGAGTATTAAAAATGTTCTTTGGTTGGTAAG  
GCCTAAGATAGGGTTTTCATTTATTTCTATACTTTTTCTGTTTTTTAAACACCTGCATATT  
TTTATGTAAATCTCTAAATTTAAATATTTTAAAGTACATTTATTTTTGGTGTTTTTATTGT  
ATAAACCTTAGACAATCAATCAGTCAGTCTTTACTGACAGGAGCAGCAGCTATCTGTCT  
TTTGCTGATCTACAAATAAATGAATTGAGAATTTAGTCCATAGAGGTCCCTGGCTACCAA  
ACACATTCTCCTTTGAATTGTTAAATTCAGAACATTCAAAATAACTGTTTTGCTACAAC  
CCATGATTATTTTCTGTTGTGTTTATTTAAATTTACTTTCTCTTTAGAAGTGCCTTAT  
TTCTGAAAATCTTAATGAAACAAACGCTTAGAACAAATATAAATATGAGACACTTGGGA  
CTACTAGAGATATTTTAGATTTTTATGAAAAAATGTGAGGGGATATTGCTGCTTTAAAA  
AGGAATAAAGTAATAAAAAATATATCTCAGCTATTTTTTTAAAGCAATATAATTCAGCAAT  
TGTCTAGAAAAGTAATCATGAGGCTACTGAGTTTGGTGTTCAGTTACTGAGTTTCAAAAA  
TGTTTTGGTGGCATGAGGACAAATTTTATTGAAGGTAAGATAAGAATAAAAACTATGTT  
TAC

SEQ ID NO: 9\_AA210825\_H

CACGAGGGCTACTGGCGCCTGGCGACCCTCCCTGCCCCCACCACAACCCGCTCCGGCAA  
CGCCCCCTTCCTCAGGCTCCCGACCGAACTTTTCTCCAACCTTCTGCGACTCGTGAGATT  
CCCTTCTACCCACTCCGGCCCTCGGGACCCCTCTGCCCATCCCTGGCCGGTCCGGTCCC  
TGCGAACCCCTTTATCTCTGGAATCCACTCGGTCCCCGACTCAGAGACTCCTGCCCTCCA  
CCCCAAGGACCCCGCCATCCTCAGGTCCCTCCGCTGCCAGATCTTTCTCGGATCCC  
CGCTCTCCACCACTGCTCAGGATCCCGCGGATCTAGAACCCAGGGTCCCCCGGGGC  
CCCCGGCGGGTCCCGGGTGGGCTCCAGGCGGGCGGTCCCCGGCCTCCCCCATGGCCAC  
CGCCCCCTCATTATCCCGCCGGGCTCCCTGGCTCTCCCGGGCCGGGTCTCCTCCGCCCC  
CCGGCGGCCTAGAGCTGCAGTCGCCGCCACCGCTACTGCCCCAGATCCCGGCCCGGGTT  
CCGGGGTCTCCTTTACATCCAGATCGGGCTGACCCGCGAGTTCTGTGCTGTTGCCCGCCG  
CCTCCGAGCTGGCTCATGTGAAGCAGCTGGCCTGTTCCATCGTGGACCAGAACTTCCCTG  
AGTGTGGCTTCTACGGCCTTTACGACAAGATCCTGCTTTTCAAACATGACCCACGTCCG  
CCAACCTCCTGCAGCTGGTGCCTCGTCCGAGACATCCAGGAGGGCGACCTGTTGGAGG  
TGGTGTGTCGGCCTCGGCCACCTTCGAGGACTTCAGATCCGCCCCGACGCCCTCACGG  
TGCACTCCTATCGGGCGCCTGCCTTCTGTGATCACTGCGGGGAGATGCTCTTCGGCCTAG  
TGCGCCAGGGCCTCAAGTGCATGGCTGCGGGCTGAACTACCACAAGCGCTGTGCCTTCA  
GCATCCCCAACAACCTGTAGTGGGGCCCGCAAACGGCGCCTGTCATCCACGTCTCTGGCCA  
GTGGCCACTCGGTGCGCCTCGGCACCTCCGAGTCCCTGCCCTGCACGGCTGAAGAGCTGA  
GCCGTAGCACCACCGAACTCCTGCCTCGCCGTCCCCCGTCATCCTCTTCTCCTCTTCTG  
CCTCATCGTATACGGGGCCGCCCATTTAGCTGGACAAGATGCTGCTCTCAAGGTCAAGG  
TGCCGCACACCTTCTCATCCACAGCTATACACGGCCACCGTTTGCCAGGCTTGCAAGA  
AACTCCTCAAGGGCCTCTTCCGGCAGGGCCTGCAATGCAAAGACTGCAAGTTTAACTGTC

## FIGURE 2H

ACAAACGCTGCGCCACCCGCGTCCCTAATGACTGCCTGGGGGAGGCCCTTATCAATGGAG  
ATGTGCCGATGGAGGAGGCCACCGATTTGAGCGAGGCTGACAAGAGCGCCCTCATGGATG  
AGTCAGAGGACTCCGGTGTGATCCCTGGCTCCCACTCAGAGAATGCGCTCCACGCCAGTG  
AGGAGGAGGAAGGCGAGGGAGGCAAGGCCAGAGCTCCCTGGGGTACATCCCCCTAATGA  
GGGTGGTGCAATCGGTGCGACACACGACGCGGAAATCCAGCACCACGCTGCGGGAGGGTT  
GGGTGGTTCATTACAGCAACAAGGACACGCTGAGAAAGCGGCACCTATTGGCGCCTGGACT  
GCAAGTGTATCACGCTCTTCCAGAACAACACGACCAACAGATACTATAAGGAAATTCGCG  
TGTCAGAAATCCTCACGGTGGAGTCCGCCAGAACTTCAGCCTTGTGCCGCCGGGCACCA  
ACCCACACTGCTTTGAGATCGTCACTGCCAATGCCACCTACTTCGTGGGCGAGATGCCTG  
GCGGGACTCCGGGTGGGCCAAGTGGGCAGGGGGCTGAGGCCGCCCGGGGGCTGGNNGAGA  
CAGCCATCCGCCAGGCCCTGATGCCCGTCATCCTTCAGGACGCACCCAGCGCCCCAGGCC  
ACGCGCCCCACAGACAAGCTTCTCTGAGCATCTCTGTGTCCAACAGTCAGATCCAAGAGA  
ATGTGGACATTGCCACTGTCTACCAGATCTTCCCTGACGAAGTGCTGGGCTCAGGGCAGT  
TTGGAGTGGTCTATGGAGGAAAACACCGGAAGACAGGCCGGGACGTGGCAGTTAAGGTCA  
TTGACAAACTGCGCTTCCCTACCAAGCAGGAGAGCCAGCTCCGGAATGAAGTGGCCATTC  
TGCAGAGCCTGCGGCATCCCGGGATCGTGAACCTGGAGTGCATGTTGAGACGCCTGAGA  
AAGTGTGTTGTGGTGATGGAGAAGCTGCATGGGGACATGTTGGAGATGATCCTGTCCAGTG  
AGAAGGGCCGGCTGCCTGAGCGCCTCACCAAGTTCCTCATCACCAGATCCTGGTGGCTT  
TGAGACACCTTCACTTCAAGAACATTGTCCACTGTGACTTGAAACCAGAAAACGTGTTGC  
TGGCATCAGCAGACCCATTTCTCAGGTGAAGCTGTGTGACTTTGGCTTTGCTCGCATCA  
TCGGCGAGAAGTCGTTCCGCCGCTCAGTGGTGGGCACGCCGGCCTACCTGGCACCCGAGG  
TGCTGCTCAACCAGGGCTACAACCGCTCGCTGGACATGTGGTCAGTGGGCGTGATCATGT  
ACGTCAGCCTCAGCGGCACCTTCCCTTTCAACGAGGATGAGGACATCAATGACCAGATCC  
AGAACGCCGCCTTCATGTACCCGGCCAGCCCCCTGGAGCCACATCTCAGCTGGAGCCATTG  
ACCTCATCAACAACCTGCTGCAGGTGAAGATGCGCAAACGCTACAGCGTGGACAAATCTC  
TCAGCCACCCCTGGTTACAGGAGTACCAGACGTGGCTGGACCTCCGAGAGCTGGAGGGGA  
AGATGGGAGAGCGATACATCACGCATGAGAGTGACGACGCGCGCTGGGAGCAGTTTGCAG  
CAGAGCATCCGCTGCCTGGGTCTGGGCTGCCACGGACAGGGATCTCGGTGGGGCCTGTC  
CACCACAGGACCACGACATGCAGGGGCTGGCGGAGCGCATCAGTGTCTCTGAGGTCCTG  
TGCCCTCGTCCAGCTGCTGCCCTCCACAGCGGTTCTTCACAGGATCCCAGCAATGAACTG  
TTCTAGGGAAAGTGGCTTCCCTGCCCAAACCTGGATGGGACACGTGGGGAGTGGGGTGGGG  
GAGCTATTTCCAAGGCCCTCCCTGTTTCCCCAGCAATTAAAACGGACTCATCTCTGGCC  
CCATGGCCTTGATCTCAGCAAAA

SEQ ID NO: 10\_AA127299\_H

ATTCAATTCAATAATTGTTGGTGCAAAAGATTTGCTTGCTATGGATTCAAATGGTCTTTCT  
GATCCTTACATCAAAATCACAAATCTTTCTCAAAAAACGAAAGTGATTAAGAAAACCTTTG  
ACTCCAACCTTGAATGAACTTTTTTTGTGCATTTTCCAGAAAAACAACCTTGAATTA  
GAATGTTGGGACCACGATACTTTTTCAGATGATTTTATTGGCAAGGCTTCCATTTCTTTG  
GCAGAGATTCCAGCTTTGGCAGAAGTTGATATGTGGATAGATATGAAAACGAAAAAGGA  
GAATTTGCAGGAAAA

SEQ ID NO: 11\_AA316804\_H

ATGTCTGCAAATAATTCCCCTCCATCAGCCCAGAAAGTCTGTATTACCCACAGCTATTCCT  
GCTGTGCTTCCAGCTGCTTCTCCGTGTTCAAGTCCTAAGACGGGACTCTCTGCCCGACTC  
TCTAATGGAAGCTTCAGTGCACCATCACTACCAACTCCAGAGGCTCAGTGCATACAGTT  
TCATTTCTACTGCAAATTGGCCTCACACGGGAGAGTGTTACCATTGAAGCCCAGGAACTG  
TCTTTATCTGCTGTCAAGGATCTTGTGTGCTCCATAGTTTATCAAAAGTTTCCAGAGTGT  
GGATTCTTTGGCATGTATGACAAAATTCCTTCTTTTCGCCATGACATGAACTCAGAAAAC  
ATTTTGCAGCTGATTACCTCAGCAGATGAAATACATGAAGGAGACCTAGTGAAGTGTT

FIGURE 21

CTTTCAGCTTTAGCCACAGTAGAAGACTTCCAGATTTCGTCCACATACTCTCTATGTACAT  
TCTTACAAAGCTCCTACTTTCTGTGATTACTGTGGTGAGATGCTGTGGGGATTGGTACGT  
CAAGGACTGAAATGTGAAGGCTGTGGATTAAATTACCATAAACGATGTGCCTTCAAGATT  
CCAAATAACTGTAGTGGAGTAAGAAAGAGACGTCTGTCAAATGTATCTTTACCAGGACCC  
GGCCTCTCAGTTCCAAGACCCCTACAGCCTGAATATGTAGCCCTTCCCAGTGAAGAGTCA  
CATGTCCACCAGGAACCAAGTAAGAGAATTCCTTCTTGGAGTGGTCGCCCAATCTGGATG  
GAAAAGATGGTAATGTGCAGAGTGAAAGTTCCACACACATTTGCTGTTCACTCTTACACC  
CGTCCCACGATATGTCAGTACTGCAAGCGGTTACTGAAAGGCCTCTTTCGCCAAGGAATG  
CAGTGTAAGATTGCAAATTCAACTGCCATAAACGCTGTGCATCAAAAGTACCAAGAGAC  
TGCCTTGGAGAGGTTACTTTCAATGGAGAACCTTCCAGTCTGGGAACAGATACAGATATA  
CCAATGGATATTGACAATAATGACATAAATAGTGATAGTAGTTCGGGGTTTGGATGACACA  
GAAGAGCCATCACCCCCAGAAGATAAGATGTTCTTCTTGGATCCATCTGATCTCGATGTG  
GAAAGAGATGAAGAAGCCGTTAAACAATCAGTCCATCAACAAGCAATAATATTCGCTA  
ATGAGGGTTGTACAATCCATCAAGCACACAAAGAGGAAGAGCAGCACAATGGTGAAGGAA  
GGGTGGATGGTCCATTACACCAGCAGGGATAACCTGAGAAAGAGGCATTATTGGAGACTT  
GACAGCAAATGTCTAACATTATTTTCAAGATGAATCTGGATCAAAGTATTATAAGGAAATT  
CCACTTTCAGAAATTCTCCGCATATCTTACCACGAGATTTCAAAACATTTCAAGGC  
AGCAATCCACACTGTTTTGAAATCATTACTGATACTATGGTATACTTCGTTGGTGAGAAC  
AATGGGGACAGCTCTCATAATCCTGTTCTTGCTGCCACTGGAGTTGGACTTGATGTAGCA  
CAGAGCTGGGAAAAAGCAATTCGCCAAGCCCTCATGCCTGTTACTCCTCAAGCAAGTGTT  
TGCACTTCTCCAGGGCAAGGGAAAGATCACAAAGATTTGTCTACAAGTATCTCTGTATCT  
AATTGTCAGATTCAAGGAGAATGTGGATATCAGTACTGTTTACCAGATCTTTGCAGATGAG  
GTGCTTGGTTCAAGGCCAGTTTGGCATCGTTTATGGAGGAAAACATAGAAAGACTGGGAGG  
GATGTGGCTATTAAAGTAATTGATAAGATGAGATTCCCCACAAAACAAGAAAGTCAACTC  
CGTAATGAAGTGGCTATTTTACAGAATTTGCACCATCCTGGGATTGTAAACCTGGAATGT  
ATGTTTGAAACCCCAAGACGAGTCTTTGTAGTAATGGAAAAGCTGCATGGAGATATGTTG  
GAAATGATTCTATCCAGTGAGAAAAGTCGGCTTCCAGAACGAATTACTAAATTCATGGTC  
ACACAGATACTTGTTGCTTTGAGGAATCTGCATTTTAAGAATATTGTGCACTGTGATTTA  
AAGCCAGAAAATGTGCTGCTTGCATCAGCAGAGCCATTTCTCAGGTGAAGCTGTGTGAC  
TTTGGATTTGCACGCATCATTGGTGAAAAGTCATTCAAGGAGATCTGTGGTAGGAACTCCA  
GCATACTTAGCCCCTGAAGTTCTCCGGAGCAAAGGTTACAACCGTTCCCTAGATATGTGG  
TCAGTGGGAGTTATCATCTATGTGAGCCTCAGTGGCACATTTCTTTTAATGAGGATGAA  
GATATAAATGACCAAATCCAAAATGCTGCATTTATGTACCCACCAAATCCATGGAGAGAA  
ATTTCTGGTGAAGCAATTGATCTGATAAACAATCTGCTTCAAGTGAAGATGAGAAAACGT  
TACAGTGTGACAAATCTCTTAGTCATCCCTGGCTACAGGACTATCAGACTTGGCTTGAC  
CTTAGAGAATTTGAACTCGCATTTGGAGAACGTTACATTACACATGAAAGTGATGATGCT  
CGCTGGGAAATACATGCATACACATAACCTTGATATACCCAAAGCACTTCATTATGGCT  
CCTAATCCAGATGATATGGAAGAAGATCCTTAA

SEQ ID NO: 12\_PKNBETA\_H

ATGGAGGAGGGGGCGCCGCGGCAGCCTGGGCGGAGCCAGTGGCCCCCAGAGGATGAGAAG  
GAGGTGATCCGCCGGGCCATCCAGAAAGAGCTGAAGATCAAGGAGGGGGTGGAGAACCTG  
CGGCGCGTGGCCACAGACCGCCGCACTTGGGCCATGTGCAGCAGCTGCTGCGGTCTCTC  
AACCGCCGCTGGAGCAGCTGCATGGCGAGCTGCGGGAGCTGCACGCCCCGAATCCTGCTG  
CCCGGCCCTGGGCCTGGCCAGCTGAGCCTGTGGCCTCAGGACCCCGGCCGTGGGCAGAG  
CAGCTCAGGGCTCGGCACCTAGAGGCTCTCCGGAGGCAGCTGCATGTGGAGCTGAAGGTG  
AAACAGGGGGCTGAGAACATGACCCACACGTGCGCCAGTGGCACCCCCAAGGAGAGGAAAG  
CTCCTTGCAGCTGCCCAGCAGATGCTGCGGGACAGCCAGCTGAAGGTGGCCCTGCTGCGG  
ATGAAGATCAGCAGCCTGGAGGCCAGTGGGTCCCCGGAGCCAGGGCCTGAGCTACTGGCG  
GAGGAGCTACAGCATCGACTGCACGTTGAGGCAGCGGTGGCTGAGGGCGCCAAGAACGTG

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FIGURE 2J

CTGAAACTGCTTAGTAGCCG SAGAAACACAGGACCGCAAGGCACTGGCTGAGGCCCAGGCC  
CAGCTACAGGAGTCTCTCAGAAACTGGAACCTCCTGCGCTTGGCTTGGAGCAGCTGCTG  
GAGCAACTGCCTCCTGCCCCACCTTTGCGCAGCAGAGTACCCCGAGAGTTGCGGGCTGCG  
GTGCTTGGATACCCCCAGCCTTCAGGGACACCTGTGAAACCCACCGCCCTAACAGGGACA  
CTGCAGGTCCGCTCCTGGGCTGTGAACAGTTGCTGACAGCCGTGCCTGGGCGCTCCCCA  
GCGGCCGCACTGGCCAGCAGCCCCCTCCGAGGGCTGGCTTCGGACCAAGGCCAAGCACCAG  
CGTGGCCGAGGCGAGCTTGCCAGTGAGGTGCTGGCTGTGCTAAAGGTGGACAACCGTGTT  
GTGGGGCAGACGGGCTGGGGGCAGGTGGCCGAACAGTCTTGGGACCAGACCTTTGTCTATC  
CCACTGGAGCGAGCCCGTGAGCTGGAGATTGGGGTACACTGGCGGGGACTGGCGGCAGCTA  
TGTGGCGTGGCCTTCTGAGACTTGAAGACTTCTTGGACAATGCCTGTCAACCAACTGTCC  
CTCAGCCTGGTACCGCAGGGACTGCTTTTTTGGCCAGGTGACCTTCTGCGATCCTGTCTATT  
GAGAGGCGGCCCCGGCTGCAGAGGCAGGAACGCATCTTCTCTAAACGCAGAGGCCAGGAC  
TTCCTGAGGCGTTTCGCAGATGAACCTCGGCATGGCGGCCTGGGGGCGCCTCGTCATGAAC  
CTGCTGCCCCCTGCAGCTCCCCGAGCACAATCAGCCCCCTAAAGGATGCCCTCGGACC  
CCAACAACACTGCGAGAGGCCTCTGACCCTGCCACTCCCAGTAATTTCTGCCCCAAGAAG  
ACCCCTTGGGTGAAGAGATGACACCCCCACCAAGCCCCCACGCCTCTACCTCCCCCAG  
GAGCCAACATCCGAGGAGACTCCGCGCACCAACAGTCCCCATATGGAGCCTAGGACTCGA  
CGTGGGCCATCTCCACCAGCCTCCCCACCAGGAAACCCCTCGGCTTCAGGACTTCCGC  
TGCTTAGCTGTGCTGGGCGGGGACACTTTGGGAAGGTCTCTCTGGTCCAGTTCAAGGGG  
ACAGGGAAATACTACGCCATCAAAGCACTGAAGAAGCAGGAGGTGCTCAGCCGGGACGAG  
ATAGAGAGCCTGTACTGCGAGAAGCGGATCCTGGAGGCTGTGGGCTGCACAGGGCACCTT  
TTCCTGCTCTCCCTCCTTGTCTGCTTCCAGACCTCCAGCCATGCCCGCTTTGTGACTGAG  
TTTGTGCTTGGTGGTGAACCTCATGATGCAGATCCACGAGGATGTCTTCCCCGAGCCCCAG  
GCCCCGCTTCTACGTGGCTTGTGTTGTCTGGGGCTGCAGTTCTTACACGAGAAGAAGATC  
ATTTACAGGGACCTGAAGTTGGATAACCTTCTGCTGGATGCCCAGGGATTCTTGAAGATC  
GCAGACTTTGGACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGT  
GGCACCCCGGAGTTCTTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACACAGGCCGTC  
GACTGGTGGGCGCTGGGTGTGCTGCTCTACGAGATGCTGGTGGGTGAGTGCCCGTTCCCA  
GGGGACACAGAGGAAGAGGTGTTTGACTGCATCGTCAACATGGACGCCCCCTACCCCGGC  
TTTCTGTGCGGTGCAAGGGCTTGAGTTCATTGAGAAGCTCCTCCAGAAGTGCCCGGAGAAG  
CGCTTCGGGGCAGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACC  
ACCAACTGGCAAGCCCTGCTCGCCCGCACCATCCAGCCCCCTTCGTGCCTACCCTGTGT  
GGCCCTGCGGACCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCTGCCCTGACC  
CCACCTGCACCCACAGCCTCCTCACTGCCCGCCAACAGGCCGCTTCCGGGACTTCGAC  
TTTGTGTGAGAGCGATTCTTGAACCCCTGA

SEQ ID NO: 13\_AI021023\_M PKNBETA\_M

GCTGAAGTGGGATAACCTTCTGCTGGATGCCCAGGGATTCTTGAAGATCGCAGACTTTGG  
ACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGTGGCACCCCGGA  
GTTCTTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACACGGGCTGTGGACTGGTGGGG  
GCTGGGTGTGCTGCTCTACGAGATGCTGGTGGGTGAGTGCCCGTTCCAGGGGACACAGA  
GGAAGAGGTGTTTGACTGCATCGTCAACATGGACGCCCCCTACCCCGGCTTTCTGTGCGT  
GCAAGGGCTTGAGTTCATTGAGAAGCTCCTCCAGAAGTGCCCGGAGAAGCGCCTCGGGGC  
GGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACCACCAACTGGCA  
AGCCCTGCTCGCCCGCACCATCCAGCCCCCTTTGTGCCTACCCTGTGTGGCCCTGCGGA  
CCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCTGCCCTGACCCACCTGCACC  
CCACAGCCTCCTCACTGCCCGCCAACAGGCCGCTTCCGGGACTTCGACTTTGTGTGAGA  
GCGATTCTTGAACCCCTGAGGGCATCTCCTGGCACCTCTGTCCCTTCCCCACAGACTG  
TTAGAGCCTCTGCTCGTTACCCGTGCGCCCTGCCTGGAGGTCCAGGCCTTGCTGGGTAC  
TTCTGAGCCCTTGGGATTCAAAGTGGCAGCCATGGGGCCACTGTTGTGGGCTTTGCTCAG

## FIGURE 2K

TGTCACTGGGCAAAGTGTGTCCCTTCCCCCTCCAGCTCGCCCTCTTCTACCTCCCAGCGA  
GACCTGGCCCAGAAAGGGTGCCGCAGCAAGGAGTGATATGCTTTGTCTTTTAAAGACTGG  
ACTTGCTTTATATTAAATTTGTAAAAGTG

SEQ ID NO: 14\_H19102\_H

GGTGGCAACATCCGGGGTCCCTGGGCCCCGAGGCTGGAAGAGCCTCTGGACAGGTTTGGGA  
ACCATCAGGTCAGATCTGGAAGAACTCTGGGAACCTACGGGGGCACCACTATCTGCACCAG  
GAATCCCTAAAGCCAGCCCCAGTACTGGTAGAGAAGCCTCTGCCAGAGTGGCCAGTGCCT  
CAGTTTCATCAACCTCTTTCTACCAGAGTTTCCCATTAGGCCCATTAGGGGGCAGCAGCAG  
CTGAAGATTTTAGGCCCTCGTGGCTAAAGGCTCCTTTTGGAACTGTCCTCAAGGTGCTAGAT  
TGCACCCAGAAAGCTGTATTTGCAGTGAAGGTGGTGCCCAAGGTAAAGGTCCTACAGAGG  
GATACCGTGAGGCAGTGCAAAGAGGAGGTTAGCATCCAGCGACAGATCAACCATCCCTTT  
GTACACAGCTTGGGGGACAGCTGGCAGGGAAAACGGCACCTTTTCATTATGTGTAGCTAC  
TGCAGCACAGATCTGTACTCCCTTTGGTCGGCTGTTGGCTGCTTTCTTGAGGCTTCCATC  
CGTCTCTTTGCTGCCGAGTTGGTGCTGGTACTGTGTTATCTCCATGACTTGGGCATCATG  
CATCGAGATGTGAAGATGGAGAATATTCTTCTAGATGAACGAGGCCATCTGAAACTGACA  
GACTTTGGTCTGTCCCGCCACGTGCCCCAGGGAGCTCAAGCCTACACTATCTGTGGCACT  
CTTCAGTACATGGCCCCAGAGGTCCTAAGTGGAGGACCTTACAACCATGCTGCTGATTGG  
TGGTCCCTGGGTGTCTTGCTTTTCTCTCTGGCGACTGGAAAGTTTCCAGTGGCTGCAGAG  
AGAGATCATGTGGCCATGTTGGCAAGTGTGACCCACAGTGACTCTGAGATCCCAGCTTCT  
CTTAACCAGGGCCTCTCACTCCTGCTCCATGAGCTCTTATGCCAGAACCCCTCCATCGT  
CTACGTTATCTGCATCACTTCCAGGTCCACCCTTTCTTTCCGGGGTGTGGCCTTCGACCCA  
GAGCTCCTACAGAAGCAGCCAGTGAACTTTGTACGGAGACACAAGCTACCCAGCCCAGT  
TCAGCGGAGACCATGCCCTTTGACGACTTTGACTGTGATCTGGAGTCCTTCTTGCTCTAC  
CCTATCCCTGCTTGA

SEQ ID NO: 15\_AA476563\_H

ATGGAATTCTTTAGGATAGACAGTAAGGATAGCGCAAGTGAACCTCCTGGGACTTGACTTT  
GGAGAAAAATTGTATAGTCTAAAATCAGAACCTTTGAAACCATTCTTTACTCTTCCAGAT  
GGAGACAGTGCTTCTAGGAGTTTAAATACTAGTGAAAGCAAGGTAGAGTTTAAAGCTCAG  
GACACCATTAGCAGGGGCTCAGATGACTCAGTGCCAGTTATTTTCGTTTAAAGATGCTGCT  
TTTGATGATGTGAGTGGTACTGATGAAGGAAGACCTGATCTTCTTGTAATTTACCTGGT  
GAATTGGAGTCAACAAGAGAAGCTGCAGCAATGGGACCTACTAAGTTTACACAACTAAT  
ATAGGGATAATAGAAAATAAACTCTTGGAAGCCCCTGATGTTTTATGCTCAGGCTTAGT  
ACTGAACAATGCCAAGCACATGAGGAGAAAGGCATAGAGGAACTGAGTGATCCCTCTGGG  
CCCAAATCCTATAGTATAACAGAGAAACACTATGCACAGGAGGATCCCAGGATGTTATTT  
GTAGCAGCTGTTGATCATAGTAGTTTCAGGAGATATGTCTTTGTTACCCAGCTCAGATCCT  
AAGTTTCAAGGACTTGGAGTGGTTGAGTCAGCAGTAAGTGCAAACAACAGAAAGAAAGC  
TTATTCGGTATTTGTAGTCCACTCTCAGGTGCTAATGAATATATTGCAAGCACAGACACT  
TTAAAAACAGAAGAAGTATTGCTGTTTACAGATCAGACTGATGATTTGGCTAAAGAGGAA  
CCAACCTCTTTATTCCAGAGAGACTCTGAGACTAAGGGTGAAAGTGGTTTAGTGCTAGAA  
GGAGACAAGGAAATACATCAGATTTTTTGAGGACCTTGATAAAAAATTAGCACTAGCCTCC  
AGGTTTTACATCCCAGAGGGCTGCATTCAAAGATGGGCAGCTGAAATGGTGGTAGCCCTT  
GATGCTTTACATAGAGAGGGAATTGTGTGCCGCGATTTGAACCCAAACAACATCTTATTG  
AATGATAGAGGACACATTGAGCTAACGTATTTTAGCAGGTGGAGTGAGGTTGAAGATTCC  
TGTGACAGCGATGCCATAGAGAGAATGTACTGTGCCCCAGAGGTTGGAGCAATCACTGAA  
GAAACTGAAGCCTGTGATTGGTGGAGTTTGGGTGCTGTCTCTTTGAACTTCTCACTGGC  
AAGACTCTGGTTGAATGCCATCCAGCAGGAATAAATACTCACACTACTTTGAACATGCCA  
GAATGTGTCTCTGAAGAGGCTCGCTCACTCATTCAACAGCTCTTGCAAGTTCAATCCTCTG

## FIGURE 2L

3AACGACTTGGTGCTGGASTTGCTGGTGTGGAAGATATCAAATCTCATCCATTTTTTTACC  
CCTGTGGATTGGGCAGAACTGATGAGATGA

SEQ ID NO: 16\_AA626690\_H

ATGCTACCATTCGCTCCTCAGGACGAGCCCTGGGACCGAGAAATGGAAGTGTTTCAGCGGC  
GGCGGCGCGAGCAGCGGCGAGGTAAATGGTCTTAAATGGTTGATGAGCCAATGGAAGAG  
GGAGAAGCAGATTCTTGTCATGATGAAGGAGTTGTTAAAGAAATCCCTATTACTCATCAT  
GTTAAGGAAGGCTATGAGAAAGCAGATCCTGCACAGTTTGAGTTGCTCAAGGTTCTTGGT  
CAGGGGTCATTTGGAAAGGTTTTTCTTGTTAGAAAGAAGACCGGTCCTGATGCTGGGCAG  
CTCTATGCAATGAAGGTGTTAAAAAAGCCTCTTTAAAGTTTCGAGACAGAGTTTCGGACA  
AAGATGGAGAGGGATATACTGGTGGAAAGTAAATCATCCATTTATTGTCAAATTGCACTAT  
GCCTTTCAGACTGAAGGGAAACTGTACTTAATACTGGATTTTCTCAGGGGAGGAGATGTT  
TTCACAAGATTATCCAAAGAGGTTCTGTTTACAGAGGAAGATGTGAAATTCTACCTCGCA  
GAACTGGCCCTTGCTTTGGATCATCTGCACCAATTAGGAATTGTTTATAGAGACCTGAAG  
CCAGAAAACATTTTGCTTGATGAAATAGGACATATCAAATTAACAGATTTTGGACTCAGC  
AAGGAGTCAGTAGATCAAGAAAAGAAGGCTTACTCATTTTGTGGTACAGTAGAGTATATG  
GCTCCTGAAGTAGTAAATAGGAGAGGCCATTCCCAGAGTGCTGATTGGTGGTCATATGGT  
GTTCTTATGTTTGAAATGCTTACTGGTACTCTGCCATTTCAAGGTAAAGACAGAAATGAG  
ACCATGAATATGATATTAAGCAAAACTTGGAATGCCTCAATTTCTTAGTGCTGAAGCA  
CAAAGTCTTCTAAGGATGTTATTCAAAGGAATCCAGCAAATAGATTGGGATCAGAAGGA  
GTTGAAGAAATCAAAGACATCTGTTTTTGCAAATATTGACTGGGATAAATTATATAAA  
AGAGAAGTTCAACCTCCTTTCAAACCTGCTTCTGGAACACAGATGATACTTTTTGTGTTT  
GATCCTGAATTTACTGCAAAAACACCTAAAGATTCTCCCGGTTTGCCAGCCAGTGCAAAT  
GCTCATCAGCTCTTCAAAGGATTGAGCTTTGTTGCAACTTCTATTGCAGAAGAATATAAA  
ATCACTCCTATCACAAGTGCAAATGTATTACCAATTGTTGAGATAAATGGAAATGCTGCA  
CAATTTGGTGAAGTATATGAATTGAAGGAGGATATTGGTGTGGCTCCTACTCTGTTTGC  
AAGCGATGCATACATGCAACTACCAACATGGAATTTGCAGTGAAGATCATTGACAAAAGT  
AAGCGAGACCCTTCAGAAGAGATTGAAATATTGATGCGCTATGGACAACATCCCAACATT  
ATTACTTTGAAGGATGTCTTTGATGATGGTAGATATGTTTACCTTGTTACGGATTTAATG  
AAAGGAGGAGAGTTACTTGACCGTATTCTCAAACAAAATGTTTCTCGGAACGGGAGGCT  
AGTGATATACTATATGTAATAAGTAAGACAGTTGACTATCTTCATTGTCAAGGAGTTGTT  
CATCGTGATCTTAAACCTAGTAATATTTTATACATGGATGAATCAGCCAGTGCAAGATTCA  
ATCAGGATATGTGATTTTGGGTTTGCAAAACAACCTTCGAGGAGAAAATGGACTTCTCTTA  
ACTCCATGCTACACTGCAAACTTTGTTGCACCTGAGGTTCTTATGCAACAGGGATATGAT  
GCTGCTTGTGATATCTGGAGTTTAGGAGTCCTTTTTTACACAATGTTGGCTGGCTACACT  
CCATTTGCTAATGGCCCCAATGATACTCCTGAAGAGATACTGCTGCGTATAGGCAATGGA  
AAATTCTCTTTGAGTGGTGGAACTGGGACAATATTTTCAGACGGAGCAAAGGATTTGCTT  
TCCCATATGCTTCATATGGACCCACATCAGCGGTATACTGCTGAACAAATATTAAAGCAC  
TCATGGATAACTCACAGAGACCAGTTGCCAAATGATCAGCCAAAGAGAAAATGATGTGTCA  
CATGTTGTTAAGGGAGCAATGGTTGCAACATACTCTGCCCTGACTCACAAGACCTTTCAA  
CCAGTCCTAGAGCCTGTAGCTGCTTCAAGCTTAGCCAGCGACGGAGCATGAAAAAGCGA  
ACATCAACTGGCCTGTAA

SEQ ID NO: 17\_AA215680\_H

ATGAGCCTGGTGGCCTGTGAGTGCCTGCCCAGCCCCGGCCTGGAGCCTGAGCCTTGCTCA  
CGAGCACGGTCCCAAGCTCACGTGTACCTGGAGCAGATTTCGCAACAGGGTGGCTCTGGGA  
GTGCCTGACATGACAAAACGTGACTATCTGGTGGATGCGGCCACGCAGATCCGGCTGGCC  
CTGGAGCGCGATGTTAGTGAGGACTATGAGGCGGCCTTCAACCACTATCAGAATGGCGTG  
GACGTGCTGCTCCGTGGCATAACGTTGACCCCAACAAGGAGCGACGTGAGGCTGTGAAG  
CTGAAAATTACCAAATACCTGCGGCGGGCAGAGGAGATCTTCAACTGCCACCTGCAGCGG

## FIGURE 2M

CCGCTGAGCAGTGGAGCCAGCCCCAGCGCGGGTTTCAGCAGCCTGAGGCTCCGGCCCCATT  
CGCACGCTGAGCTCTGCCGTGGAGCAGCTGAGGGGCTGCAGGGTGGTCCGGGGTCATCGAG  
AAGGTGCAGCTGGTCCAGGACCCGGCAACCGGAGGGACCTTTGTGGTGAAGAGCCTACCC  
AGGTGCCACATGGTGAAGCAGGAGCGGCTGACCATCATCCCAACGGAGTCCCCCTACATG  
ACGAAGCTGCTCAGGTACTTTGTGAGCGAGGACTCCATCTTCTGACCTGGAGCATGTG  
CAAGGAGGCACTCTCTGGTCCCACCTGCTCTCCCAGGCGCACTCCCGACATTCTGGGCTC  
AGCTCTGGCTCTACCCAGGAGAGGATGAAGGCTCAGCTCAACCCCCACCTCAACCTCCTG  
ACCCCAGCGAGGCTTCCCTCAGGCCATGCCCCCTGGCCAGGACAGAATCGCCCTGGAGCCT  
CCTAGGACTTCTCCGAACCTTCTCCTAGCTGGGGAGGCCCCATCCACCAGACCCCAGAGG  
GAGGCTGAAGGTGAACCCACAGCCAGGACCAGCACCTCTGGCTCCTCGGACCTTCCAAAG  
GCCCCAGGTGGCCACCTGCACCTTCAAGCTAGGAGGGCTGGCCAGAACTCAGACGCTGGG  
CCCCCTCGGGGGCTCACTTGGGTTCTGAGGGGGCCGGCCCCGGTGCTAGGGGGGCTGTGGC  
CGAGGCATGGATCAGAGCTGCCTGTGAGCAGATGGGGCCGGCCGGGGCTGTGGCAGGGCC  
ACCTGGAGTGTGAGAGAGGAGCAGGTGAAGCAGTGGGCGGCAGAGATGCTGGTAGCGCTG  
GAGGCGCTGCACGAGCAGGGGGTGCTGTGCCGGGACCTCCACCCCGGGAACCTGCTCCTG  
GACCAGGCAGGTACATCCGGCTCACATATTTTGGCCAGTGGTCAGAGGTGGAGCCCCAG  
TGCTGCGGGGAGGCCGTGGACAATCTCTACAGCGCCCCAGAGGTGGGTGGGATTTCCGAG  
CTGACGGAAGCCTGTGACTGGTGGAGCTTTGGGTCTCTACTGTATGAACTGCTGACGGGA  
ATGGCACTGTCCAGAGCCACCCTTCAGGAATCCAGGCCACACCCAGCTCCAGCTGCCC  
GAGTGGCTCAGTCGCCCAGCGGCTCTCTGCTGACTGAGCTGCTGCAGTTCGAGCCTACC  
CGGCGCCTGGGCATGGGAGAAGGTGGTGTGAGCAAACTCAAGTCCCATCCCTTTTTCAGT  
ACCATCCAATGGAGCAAGCTGGTGGGGTAA

SEQ ID NO: 18\_SGK\_H

ATGACGGTGAAAACTGAGGCTGCTAAGGGCACCTCACTTACTCCAGGATGAGGGGCATG  
GTGGCAATTCTCATCGCTTTCATGAAGCAGAGGAGGATGGGTCTGAACGACTTTATTTCAG  
AAGATTGCCAATAACTCCTATGCATGCAAACACCCTGAAGTTCAGTCCATCTTGAAGATC  
TCCCAACCTCAGGAGCCTGAGCTTATGAATGCCAACCCTTCTCCTCCACCAAGTCCTTCT  
CAGCAAATCAACCTTGGCCCCGTCGTCCAATCCTCATGCTAAACCATCTGACTTTCACTTC  
TTGAAAGTGATCGGAAAGGGCAGTTTTTGGAAAGGTTCTTCTAGCAAGACACAAGGCAGAA  
GAAGTGTTCTATGCAGTCAAAGTTTTACAGAAGAAAGCAATCCTGAAAAAGAAAGAGGAG  
AAGCATATTATGTGCGAGCGGAATGTTCTGTTGAAGAATGTGAAGCACCTTTCTCTGGTG  
GGCCTTCACTTCTCTTTCCAGACTGCTGACAAATTGTACTTTGTCTTAGACTACATTAAT  
GGTGGAGAGTTGTTCTACCATCTCCAGAGGGAACGCTGCTTCTGGAACCACGGGCTCGT  
TTCTATGCTGCTGAAATAGCCAGTGCCCTGGGCTACCTGCATTCACTGAACATCGTTTAT  
AGAGACTTAAAACCAGAGAATATTTTGCTAGATTACAGGGACACATTGTCTTACTGAT  
TTCGGACTCTGCAAGGAGAACATTGAACACAACAGCACAAACATCCACCTTCTGTGGCAGC  
CCGGAGTATCTCGCACCTGAGGTGCTTCATAAGCAGCCTTATGACAGGACTGTGGACTGG  
TGGTGCCTGGGAGCTGTCTTGTATGAGATGCTGTATGGCCTGCCGCCTTTTTATAGCCGA  
AACACAGCTGAAATGTACGACAACATTCTGAACAAGCCTCTCCAGCTGAAACCAATATT  
ACAAATTCCGCAAGACACCTCCTGGAGGGCCTCCTGCAGAAGGACAGGACAAAGCGGCTC  
GGGGCCAAGGATGACTTCATGGAGATTAAGAGTCATGTCTTCTTCTCCTTAATTAAGTGG  
GATGATCTCATTAATAAGAAGATTACTCCCCCTTTTAAACCCAAATGTGAGTGGGCCCCAAC  
GAGCTACGGCACTTTGACCCCCGAGTTTACCGAAGAGCCTGTCCCCAACTCCATTGGCAAG  
TCCCCTGACAGCGTCCTCGTCACAGCCAGCGTCAAGGAAGCTGCCGAGGCTTTCTTAGGC  
TTTTCTATGCGCCTCCACGGACTCTTTCCTCTGA

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CGGGTCGACCCACGCGTCCGCCGGTTTCACTGCTCCCCTCAGTCTCTTTTGGGCTCTTTC  
CGGGCATCGGGACGATGACCGTCAAAGCCGAGGCTGCTCGAAGCACCTTACCTACTCCA

GAATGAGGGGGAATGTTAGCGATTCTCATCGCTTTTATGAAACAGAGAAGGATGAGGCGCTGA  
ACGATTTTATTTCAGAAGATTGCCAGCAACACCTATGCATGCAAACACGCTGAAGTTCAGT  
CCATTTTGA AAAATGTCCCATCCTCAGGAGCCGAGCTTATGAACGCTAACCCCTCTCCTC  
CGCCAAGTCCCTCTCAACAAATCAACCTGGGTCCGTCTCCAACCCCTCACGCCAAACCCCT  
CCGACTTTTCACTTCTTGAAAGTGATCGGAAAGGGCAGTTTTTGAAAGGTTCTTCTGGCTA  
GGCACAAGGCAGAAGAAGTATTCTATGCAGTCAAAGTTTTACAGAAGAAAGCCATCCTGA  
AGAAGAAAGAGGAGAAGCATATTATGTCAGAGCGGAATGTTCTGTTGAAGAATGTGAAG  
ACCCTTTTCTGGTGGGCGCTTCACTTCTCATTCCAGACCGCTGACAAGCTCTACTTTGTCC  
TGGACTACATTAATGGTGGAGAGCTGTTCTACCATCTCCAGAGGGAGCGCTGCTTCCTGG  
AACCACGGGCTCGATTCTACGCAGCTGAAATAGCCAGTGCCTTGGGCTATCTGCACTCCC  
TAAACATCGTTTTATAGAGACTTAAAACCTGAGAATATTCTCCTAGACTCCCAGGGGGCACA  
TCGTCTCACTGACNTATTTAGCTGCGTAGAATCGAGCATAACGGGACAACATCTACCT  
TCTGTGGCAGCGCTGAGTATCTGGCTCCTGAGGTCCTCCATAAGCAGCCGTATGACCGGA  
CGGTGGACTGGTGGTGTCTTGGGGCTGTCTGTATGAGATGCTCTACGGCCTGCCCCCGT  
TTTATAGCCGGAACACGGCTGAGATGTACGACAATATTCTGAAACAAGCCTCTCCAGTTGA  
AACC AAATATTACAAACTCGGCAAGGCACCTCCTGGAAGGCCTCCTGCAGAAGGACCGGA  
CCAAGAGGCTGGGTGCCAAGGATGACTTTATGGAGATTAAGAGTCATATTTTCTTCTCTT  
TAATTAAGTGGGATGATCTCATCAATAAGAAGATTACACCCCATTTAACC CAAATGTGA  
GTGGGCCCAGTGACCTTCGGCACTTCGATCCCGAGTTTACCGAGGAGCCGGTCCCCAGCT  
CCATCGGCAGGTCCCCTGACAGCATCCTTGTCACGGCCAGTGTGAAGGAAGCAGCAGAAG  
CCTTCCTCGGCTTCTCCTATGCACCTCCTGTGGATTCTCTCCTCTGAGTGCTCCCGGGAT  
GGTTCTGAAGGACTTCCTCAGCGTTTCCTAAAGTGTTTTTCGTTAGCCTTTGGTGGAGTTG  
CCAGCTGACAGAACATTTTAAAGAATTTGCACACCTGGAAGCTTGGCAGTCTCGCCTGC  
CCGGCGTGCGCGACGCAGCGCGCGCTGCTTGATGGGAGCTTTCCGAAGAGCACACCCTC  
CTCTCAATGAGCTTGTGAGGTCTTCTTTTCTTCTTCTTCTTCCACGTTGGTGCTAGCTCC  
AGGCGAGCGAGCGTGAGAGTGCCGCCTGAGACAGACACCTTGGTCTCAGTTAGAAGGAAG  
ATGCAGGTCTAAGAGGAATCCCCGCAGGTCTGTCTGAGCTGTGATCAAGAATATTCTGCA  
ATGTGCCTTTTCTGAGATCGTGTTAGCTCCAAAGCTTTTTCCTATCGCAGAGTGTTAGT  
TTGTGTTTTGTTTGTGTTTTGTTTTGTTTTGTTTTTCCCTTGGCGGATTTCCCGTGTGTGCA  
GTGGCGTGAGTGTGCTATGCCTGATCACAGACGGTTTTTGTGTGTGAGCATCAATGTGACAC  
TTGCAAGGACACTACAATGTGGGACATTGTTTGTGTTTCTTCCACATTTGGAAGATAAATTTA  
TGTGTAGACTGTTTTGTAAGATATAGTTAATAACTAAAACCTATTGAAACGGTCTTGCAA  
TGACGAGCATTTCAGATGCTTAAGGAAAGCATTGCTGCTACAAATATTTCTATTTTTTAGAA  
AGGGTTTTTATGGACCAATGCCCCAGTTGTCAGTCAAAGCCGTTGGTGTTTTTCATTGTTT  
AAAATGTCACCTATAAAACGGGCATTATTTATGTTTTTTTTTCCCTTTGTTTCATATTCTTT  
TGCATTCTGATTATTGTATGTATCGTGTAAGGAAGTCTGTACATTGGGTTATAACACT  
AGATATTTAAACTTACAGGCTTATTTGTAAACCATCATTTTAATGTACTGTAATTAACAT  
GGGTTATAATATGTACAATTCCTCCTCCTTACCACACAACCTTTTTTTGTGTGCGATAAAC  
CAATTTTGGGTTTGCAATAAAATCTTGAAAACCT

CCACCTGCAGCGGGAGCGCCGGTTCTTGAGCCCCGGGCCAGGTTCTACGCTGCTGAGGT  
GGCCAGCGCCATTGGCTACCTGCACTCCCTCAACATCATTTACAGGGATCTGAAACCAGA  
GAACATTCTCTTGGA CTGCCAGGGACACGTGGTGCTGACGGATTTTGCCCTCTGCAAGGA  
AGGTGTAGAGCCTGAAGACACCACATCCACATTCTGTGGTACCCCTGAGTACTTGGCACC  
TGAAGTGCTTCGGAAAGAGCCTTATGATCGAGCAGTGGACTGGTGGTGCTTGGGGGCAGT  
CCTCTACGAGATGCTCCATGGCCTGCCGCCCTTCTACAGCCAAGATGTATCCCAGATGTA  
TGAGAACATTCTGCACCAGCCGCTACAGATCCCCGGAGGCCGGACAGTGGCCGCCTGTGA  
CCTCCTGCAAAGCCTTCTCCACAAGGACCAGAGGCAGCGGCTGGGCTCCAAAGCAGACTT  
TCTTGAGATTAAAGAACCATGTATTCTTCAGCCCCATAAACTGGGATGACCTGTACCACA



## FIGURE 20

GAGGCTAACTCCACCCTTCAACCCAAATGTGACAGGACCTGCTGACTTGAAGCATTTTGA  
CCCAGAGTTCACCCAGGAAGCTGTGTCCAAGTCCATTGGCTGTACCCCTGACACTGTGGC  
CAGCAGCTCTGGGGCCTCAAGTGCATTCTCTGGGATTTTCTTATGCGCCAGAGGATGATGA  
CATCTTGGATTGCTAGAAGAGAAGGACCTGTGAACTACTGAGGCCAGCTGGTATTAGTA  
AGGAATTACCTTCAGCTGCTAGGAAGAGCGACTCAAATAACAATGGCTTCAACGAGAAG  
CAGGTTTATTTTTTCCAGCACATAAAAGAAAAATAATGTTTCGGAGTCCAGGACTGGCAG  
GACAGGTCATCAGATACTCAGAGGCTGTATCTCTGCCCTGCCAACCTTGACAAATGGCTT  
CCAATGTTAGGTTTGCTACAAGATGGTTACTGGAGCTCTAGCTGCCTATTTTGTGTTTAG  
GGAAGGGAAAATGGAGGAAAGGGGAGAAGAGCAAAGGGCGCTTTTAAAGAGCTTTCCCAA  
AAGCTCCACCCAATGACTTCTGCTTCCATCTCACTAACCACCCACCCCTACCTGGAATGG  
AGGCTGGGAGATGTGGCTTATTTGCTGGGTACGTGACTATCCCTAATAACAAAGGGGTTC  
TGACACTAAGACATTAGGGGAGAATGTTGGGTAGGCAGCCAGCACTCTTTTACCAGAGGG  
CCTCCTGGTGTGTTGGATTTTGATCTCAATGTGTAAAATGACAGAGATGTAACAAGCTCAT  
AGGGTATCAATATCTCTTATTGTTCT

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CGGATGCATTTNTTGGTGTGCTCTTGAGGGATTAAATGCAAAGAGATCACACCATGGACT  
ACAAGGAAAGCTGCCCAAGTGTAAGNATTCCCAGCTCCGATGAACACAGAGAGAAAAAGA  
AGAGGTTTACTGTTTATAAAGTTCTGGTTTCAGTGGGAAGAAGTGAATGGTGTGCTTCA  
GGAGATATGCAGAGTTTGATAAACTTTATAACACTTTAAAAAACAGTTTCTGCTANGG  
CCCTGAAGATTCCTGCCAAGAGAATATTTGGTGATAATTTTGATCCAGATTTTATTAAAC  
AAAGACGAGCAGGACTAAACGAATTCATTGAGAACCTAGTTAGGTATCCAGAACTTTATA  
ACCATCCAGATGTCAGAGCATTCTTCAAATGGACAGTCCAAAACACCAGTCAGATCCAT  
CTGAAGATGAGGATGAAAGAAGTTCTCAGAAGCTACACTCTACCTCACAGAACATCAACC  
TGGGACCGTCTGGAAATCCTCATGCCAAACCAACTGACTTTGATTTCTTAAAAGTTATTG  
GAAAAGGCAGCTTTGGCAAGGTTCTTCTTGCAAAACGGAAACTGGATGGAAAATTTTATG  
CTGTCAAAGTGTTACAGAAAAAATAGTTCTCAACAGAAAAGAGCAAAAACATATTATGG  
CTGAACGTAATGTGCTCTTGAAAAATGTGAAACATCCGTTTTTGGTTGGATTGCATTATT  
CCTTCCAAACAACCTGAAAAGCTTTATTTTGTCTGGATTTTGTAAATGGAGGGGGAGGGAC  
ATGTTGTCTTAAACAGATTTTGGGCTTTGTAAAGAAGGAATTGCTATTTCTGACACCACTA  
CCACATTTTGTGGGACACCAGAGTATCTTGACCTGAAGTAATTAGAAAACAGCCCTATG  
ACAATACTGTAGATTGGTGGTGCTTGGGGCTGTTCTGTATGAAATGCTGTATGGATTGC  
CTCCTTTTTTATTGCCGAGATGTTGCTGAAATGTATGACAATATCCTTCACAAACCCCTAA  
GTTTGAGGCCAGGAGTGAGTCTTACAGCCTGGTCCATTCTGGAAGAACTCCTAGAAAAAG  
ACAGGCAAAATCGACTTGGTGCCAAGGAAGACTTCTTGAAATTCAGAATCATCCTTTTTT  
TTGAATCACTCAGCTGGGCTGACCTTGTACAAAAGAAGATTCCACCACCATTTAATCCTA  
ATGTGGCTGGACCAGATGATATCAGAACTTTGACACAGCATTACAGAAGAAACAGTTC  
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TTTGCCATTGAGAAACCATTGAGCAAAATAAGTCTATAGATGGGACTGAACTTCTATTT  
GTGTGAATATATTCAAATATGTATACTAGTGCCTCATTTTTTATATGTAATGATGAAAAC  
TATGAAAAAATGTATTTTCTTCTATGTGCAAGAAAAATAGGGCATTTCAAAGAGCTGTTT  
TGATTAATAATTTATATTCTTGTTTAATAAGCTTATTTTAAACAATTTAAAGCTATTAT  
TCTTAGCATTAACCTATTTTTTAAAGAAACCTTTTTTGGCTATTGACTGTTTTTCCCTCTA  
AGTTTACACTAACATCTACCCAAGATAGACTGTTTTTTAACAGTCAATTTAGTTCAGCT  
AACATATATTAATACCTTTGTAACCTTTGCTATGGCTTTTGTATCACACCAAAACTAT  
GCAATTGGTACATGGTTGTTTAAGAAGAAACCGTATTTTTCCATGATAAATCACTGTTTG  
AAATATTTGGTTTCATGGTATGATCGAAATGTAAAAGCATAATTAACACATTGGCTGCTAG  
TTAACAATTGGAATAACTTTATTCTGCAGATCATTTAAGAAGTAACAGGCCGGGCGCGGT  
GGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGCGGGCAGATCACCTGAGGTCA

## FIGURE 2P

GGAGTTGGAGAGCCAGCCTGACCAACA'TGGACAAACCCCGTCTCTACTAAAAATACAAAAT  
TGGCAGGGTGTGGTGGCACATGCCTATAATCCCAGCTACTTGGGAGGCTAAGGCAGGAGA  
ATCGCTTGAACCCGGGAGGCGGAGGTTGCASTGAGCCGAGATCGCACCATTGCACTCCTG  
CCTGGGCAACAAGAGTGAAACTCCATCTCC

SEQ ID NO: 22\_R47805\_H

ATGGCGCACCAAACGGGCATCCACGCCACGGAAGAGCTGAAGGAATTCTTTGCCAAGGCA  
CGGGCTGGCTCTGTGCGGCTCATCAAGGTTGTGATTGAGGACGAGCAGCTCGTGCTGGGT  
GCCTCGCAGGAGCCAGTAGGCCGCTGGGATCAGGACTATGACAGGGCCGCTGCTGCCACTG  
CTGGACGCCCAGCAGCCCTGCTACCTGCTCTACCGCCTCGACTCACAGAATGCTCAGGGC  
TTCGAATGGCTCTTCCTCGCCTGGTGCCTGATAACTCCCCCGTGCGGCTGAAGATGCTG  
TACGCGGCCACGCGGGCCACAGTGAAAAAGGAGTTTGGAGGTGGCCACATCAAGGATGAG  
CTCTTCGGGACTGTGAAGGATGACCTCTCTTTTGCTGGGTACCAGAAACACCTGTCTGTC  
TGTGCGGCACCTGCCCCGCTGACCTCGGCTGAGAGAGAGCTCCAGCAGATCCGCATTAAC  
GAGGTGAAGACAGAGATCAGTGTGGAAAGCAAGCACCAGACCCTGCAGGGCCTCGCCTTC  
CCCCTGCAGCCTGAGGCCAGCGGGCACTCCAGCAGCTCAAGCAGAAAATGGTCAACTAC  
ATCCAGATGAAGCTGGACCTAGAGCGGGAAACCATTGAGCTGGTGCACACAGAGCCCACG  
GATGTGGCCCAGCTGCCCTCCCGGGTGCCCCGAGATGCTGCCCGCTACCACTTCTTCCTC  
TACAAGCACACCCATGAGGGCGACCCCCCTTGAGTCTGTAGTGTTTCATCTACTCCATGCCG  
GGGTACAAGTGCAGCATCAAGGAGCGAATGCTCTACTCCAGCTGCAAGAGCCGCCTCCTC  
GACTCCGTGGAGCAGGACTTCCATCTGGAGATCGCCAAGAAAATTGAGATTGGCGATGGG  
GCAGAGCTGACGGCAGAGTTCTCTACGACGAGGTGCACCCCAAGCAACACGCCTTCAAG  
CAGGCCTTCGCCAAGCCCAAGGGCCAGGGGCAAGCGGGGCCATAAGCGCCTCATCCGC  
GGCCCCGGGTGAAAATGGGGATGACAGCTAG

SEQ ID NO: 23\_H60215\_H

CCACGCGTCCGGCGCCCGCAGCCATGGAGGGAGGCGGCGGCGGCGGCGGCGGCTCGGG  
TGGCTGCGCTGGGAGGCGGCGGTGAGAGGCTCGCACGCCTCCAGCCCCGGCCCCCG  
CGGGAGGGAGAGCCGAGCAGCCCCGGCTCTGGGCTACGGACTATGGGCGAATAGCTCTGA  
CCACCCGGCGAAGTGCACACACCCAGAAGCTATGTCTTTCGGCAGTAAAGTTTACAGC  
ACAATATATGTGCTCTGCTCTCCTCCCGCAATCCTGCTCCAAGAGATCTTAAGCTGGAGG  
CACCAGGTCTGAATTCCAGACTCCTCCCCACCACCCACACTTCACCTCCAAGTGGAGCAT  
GACCACAGACCCATTGAGGGAGGCTGGCGGACTCTTCATCCTGGACAGTCCCTTACTGTA  
TGTCAAAGCTGAGAATGAAGCGGAGAGCATCAGACAGAGGAGCTGGGGAAACGTCGGCCA  
GGGCCAAGGCTCTAGGAAGTGGGATTTCTGGAAATAATGCAAAGAGAGCTGGACCATTCA  
TCCTTGGTCCCCGCTCTGGGCAACTCACCGGTGCCAAGCATAGTGCAGTGTGTTGGCGAGGA  
AAGATGGCACGGATGACTTCTATCAGCTGAAGATCCTGACCCTGGAGGAGAGGGGGGACC  
AAGGCATAGAGAGCCAGGAAGAGCGGCAGGGCAAGATGCTGCTGCACACCGAGTACTCAC  
TGCTGTCTCTCCTGCACACGCAGGATGGCGTGGTGCACCACCACGGCCTCTTCCAGGACC  
GCACCTGTGAAATCGTTGAGGACACAGAATCCAGCCGGATGGTTAAGAAGATGAAGAAGC  
GCATCTGCCTCGTCCTGGACTGCCTCTGTGCTCATGACTTCAGCGATAAGACCGCTGACC  
TCATCAACCTGCAGCACTACGTCATCAAGGAGAAGAGGCTCAGCGAGAGGGAGACTGTGG  
TAATCTTCTACGACGTGGTCCGCGTGGTGGAGGCCCTGCACCAGAAAAATATCGTGCACA  
GAGACCTGAAGCTGGGGAACATGGTGCTCAACAAGAGGACACATCGGATAACCATCACCA  
ACTTCTGCCTCGGGAAGCATCTGGTGAGCGAGGGGGACCTGCTGAAGGACCAGAGAGGGA  
GCCCTGCCTACATCAGTCCCGACGTGCTCAGCGGGCCGGCCGTACCGTGCGCAAGCCAGTG  
ACATGTGGGGCCCTGGGCGTGGTGTCTTCCACCATGCTGTATGGCCAGTTCCCCTTCTACG  
ACAGCATCCCGCAGGAGCTCTTCCGCAAGATCAAGGCTGCCGAGTATACCATTCCTGAGG  
ATGGACGGGTTTCTGAGAACACCGTGTGTCTCATCCGGAAGCTGCTGGTTCCTTGACCCCC  
AGCAGCGCCTGGCCGCCGCCGACGTCCTGGAGGCCCTCAGTGCCATCATTTGCATCATGGC

## FIGURE 2Q

AGTCCCTGTCATCTCTGAGTGGGCCTTTGCAAGTGGTTCTTGACATTGATGACCAAATGA  
GCAATGCGGATAGCTCCCAGGAGGCGAAGGTGACGGAGGAGTGCTCCCAGTACGAGTTTG  
AGA ACTACATGCGTCAGCAGCTGCTGCTGGCCGAGGAGAAGAGCTCCATCCATGACACCC  
GGAGCTGGGTACCCAAGCGGCAGTTCGGCAGCGCACCCACCGGTGCGACGGCTGGGCCACG  
ACGCACAGCCCATGACCTCCTTGGACACGGCCATCCTGGCGCAGCGCTACCTGCGGAAAT  
AACAGCCTCAGCCGGGGCCACCAGCACTGCTGCCACTTCTTCCAGCCCCAGCCAAAGGCC  
TGGCTGTCAGGGCTGGGCCCTGTAGTGCTGGACTCTCCCGGGCCACAATAGGGACAGGGC  
AGGGACAGGGACAGCCCAGGTACACAGTGGGGTCAGCAGAGGTACCACGAAGCTACCTTT  
TGGGATGATTGCTCGATTGTTTGGTTTTTAAATCTGAGAAGCCTAGATAACTAATCTGCT  
TTTAATCACGATGTTTTAATCTACCTCTGTCTCTTTAACCATGCTGTCTCTGGACTGAGC  
AAGAGGGAGGAGGGAGCCTGCTCACCCCACTCCAGGGCCTTCCCCAGCGGCCACCAACTG  
ACCTGGGGCGCTGCTCCCCACAGTCCAAATAAGCTGAAAGTGCAGCTCGCTGCAGGCCCC  
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CAA ACTCAAATATATTTATTTTTTTTACCAT

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GCCGCGATGGCCAGCACCAGGAGTATCGAGCTGGAGCACTTTGAGGAACGGGACAAAAGG  
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CCCAAGGGGAACGGGCTCATCCCCAGTCCGGCGCACAGTGCCCACTGCAGCTTCTACCGC  
ACGCGGACCCTGCAGGCCCTCAGCTCGGAGAAGAAGGCCAAGAAGGCGCGCTTCTACCGG  
AACGGGGACCGCTACTTCAAGGGCCTGGTGTGTGCCATCTCCAGCGACCGCTTCCGGTCC  
TTCGATGCGCTCCTCATAGAGCTCACCCGCTCCCTGTGCGGACAACGTGAACCTGCCCCAG  
GGTGTCCGCACTATCTACACCATCGACGGCAGCCGGAAGGTACCAGCCTGGACGAGCTG  
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TCAGGAGTCGTCAAGAGGCTCTGCACCCTGGATGGAAAGCAGGTGAGAGTTACGTGTGTG  
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TGTGGCACACCCACTTATGTGGCTCCARAAATCATTGCTGAAACTGGCTATGGCCTGAAG  
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CGAAGTGAGAACAATCTCCAGGAAGATCTCTTCGACCAGATCTTGGCTGGGAAGCTGGAG  
TTTCCGGCCCCCTACTGGGATAACATCACGGA CTCTGCCAAGGAATTAATCAGTCAAATG  
CTTCAGGTAAATGTTGAAGCTCGGTGTACCGCGGGACAAATCCTGAGTCACCCCTGGGTG  
TCAGATGATGCCTCCCAGGAGAATAACATGCAAGCTGAGGTGACAGGTAAACTAAAACAG  
CACTTTAATAATGCGCTCCCCAAACAGAACAGCACTACCACCGGGGTCTCCGTCTATCATG

## FIGURE 2R

GTGAGTGGGAAGGCGGCAGGTCTGGCCTGACTGCGGAGCCGGCCTTGAAGTTTTTGAATTA  
 GGTAGCCGGGAGCTGCCCTCACATGGAAGTTGGTGCCTTCCGTAGTCCTATTTTCATATGA  
 AGATTGGCTTGGCATGTGGAGGGCACTCATTGCGCAACTCCCAGGCTTTGGGCACTGTGT  
 GGAGGGGCTTGTGTAGGGACCAGCAGGCCTGGTGTGAGGGGTCCAGGCGTCAAGGAGCTC  
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 CTCCCAAGCCCTGGAGGGTGTGTTGTGTTAGGAATTAACCTCCCTGCCTACCCCAAGGCC  
 TCAGAAATAGATTATTAGAGATGTGAATTATTCTTTGAGACTTGGGATAAGAAACAGCCA  
 AAGCTAAACATATTTTCAGTTTTTAAAAAATCAGTGTTTTATAAAACACAGTTTGGGGCTTT  
 TAAAGGTACATAATCAAGGAAAAAATATATATTCATTTTTTCAGGGTTGGTAACATTTTA  
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 TCTTAAGGCAACTCTCCTAAATACATAAAACACAACAAATTAATAAGTGAAGTGACATGAG  
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 GCTGTCCAGGCCTGAGCCAATGCAACCCTGGGCGGGAAGGCCAGCTCACCGTGAGCAGGT  
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 GGAACAGGGGTGGAGTGGCCTTTCCCAGAGCTGGAGTTGGCTGCAGCAGCTTTCGAATCA  
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 TCCTGACAGCTAAGGATGGGCCACCTCCACAGCTCCGTCCTACTCGTACTTGGGACAGGCCT  
 CTCATCCTCTGGGAAGGTCTCCTTGTTCCTACCCAACTAGAAGGGAAACAGTGGCATA  
 TTCTCATGGTACATGGTTGTCTGAAAGCCTTACCTAGGAAGACGCAGGGTCTAGATAGAA  
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ACCAAGTCCTCCAGCTCCTCTCCAACCAGCCCGGGAAGTTTCAGAGGATTGAAGATTTCT  
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 CTGATTGAGAACGAAGTGTCAATCCTGCGCCGAGTGAAGCACCCCAACATCATCATGTTG  
 GTTGAAGAGATGGAAACAGCAACTGACCTCTTCTAGTGATGGAAGTGGTCAAAGGTGGA  
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 GTGTACAACCTAGCCAATGCCCTCCGGTACCTGCACAGCCTCAGCATCGTCCACAGGGAC  
 ATCAAGCCTGAGAACTCTGCTGGTGTGCGAATACCCAGATGGAACCAAGTCTTTGAAGCTG  
 GGAGACTTTGGGCTGGCGACGGTGGTTGAAGGCCCGTTGTACACGGTCTGTGGCACGCCA  
 ACTTATGTGGCACCAGAGATCATAGCTGAAACAGGTTATGGCCTGAAGGTGGATGTTTGG  
 GCAGCTGGTGTGATTACATACATACTTCTCTGTGGATTCCCACCATTTCCGGAGTGAGAAC  
 AATCTCCAGGAAGATCTCTTTGACCAGATCTTGGCTGGAAAGCTGGAATTCCCAGCCCCC  
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CCAGCAGCCAAGAGGGTAGTGGTGTACCGGAATGGGGACCCATTCTTCCCAGGCTCCCAG  
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 ACCAACCTGGCAGACTTGAAGAACAGAGGGCAGTATGTGGCCGCTGGATTTGAACGATTC

## FIGURE 2S

CACAAGCTCCCCCCTTACCAGGCTTTTTGTCTCAGTGTGTTTCAGGAATGGGGACCTGGTA  
AGTCCCCCATTTAGTCTGAAGCTGTCCCAGGCTGCCAGCCAGGACTGGGAAACTGTCTTG  
AAGCTCCTGACTGAGAAGGTCAAGTTGCAGAGTGGGGCTGTGAGACTCTGCACCCTAGAG  
GGGCTCCCCTGTGTCAGCAGGGAAGGAGCTGGTAACTGGCCATTACTATGTGGCTGTGGGA  
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GGCAATGAAGCCCACCTGAGGAGTGGAGTGGGGACTGTGCTGGTTCCCCCAAGCCTCTT  
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CAAGATGACTTTGTCTGATCATAGTCGTGACGGCTCCTGAGAGAGCACCAGGCGGGC  
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CCCATGGGCATCATTGCCGCCAATGTGGAAAAGCATTATGAGACTGGCCGGGTCTATTGGG  
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CTCTTTAACATCATCCAGCTGGGCCACTTTGAGTTCCTCCCCCTTACTGGGACAATATC  
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ACAGCTCATCAGGTTCTTCAGCACCCCTGGATCGAAACAGCTGGCAAGACCAATACAGTG  
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AAGGACAGAGAAAAGGATAGAAGTTTGAGAGAAAAACAATGAAAGAGGCTTCTTCACATA  
ATTGGTGAATCAGAGGGAGAGACACTGAGTATATTTTAAAGCATATTAAAAAAATTAAGT  
CAATGTAAATGTCAACATATTTTTAGATTTGTATATTTAAAGCCTTTAATACATTTT  
TGGGGGGTAAGCATTGTCTCAGTGAGGAATTTTGGTAATAATGATGTGTTTTGCTTCCC  
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CTGTGAGATTAATAAGGTGCATTG

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CAGAGCAGCCTCCACTCAGTCCGCGCAGAGCACAGCCCACTGAAGCCCAGGGTGGTGACG  
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GACTTCTTCCGGGAGGGTGTATGCTTTTCATAGCTATGGGCAAAGAGCCGCTGACATTGAAG  
AGTATCCAGTTGGCCATGGAGGAGCTGTATCCTAAGAACCGGGCTCTTGCCCTGGCCCCCT  
CACAGTAGAGTCCCCTCCCCAAGGCTGAGAAGCAGACTTCCCAGCAAGCTTCTGAAAGGA

FIGURE 2T

AGTCACCGCTGTGGGGAGGCAGGAAGCTATAGCGCGGAAATGGAGAGTAAGGCAGTCTCT  
AGGCATCAGGGCAAGACTTCCACAGTGCTGGCCCCAGAAGACAAGGCGAGGGCCCAGAAG  
TGGGTAAGAGGGGAAACAGGAGTCAGAACCTGGTGGCCCCGCCTTACCCGGGGCAGCCACT  
CAGGAGGAGACTCATGCAAGTGGAGAGAAACATCTGGGGGTGGAGATCGAAAAGACCTCC  
GGGGAGATTGTGAGATGTGAGAAGTGTAAAGAGAGAAAGAGAGCTGCAGTTGGGCCTGCAG  
AGGGAGCCGTGCCCCGCTGGGAACCAAGTGCAGCTGGACCTGGGGAGAGCTCAGAAGAGGGAT  
TCCGAGAAGTTGGTGAGGACCAAGAGCTGCAGGAGGCCTTCTAAGGCAAAATTTACAGAT  
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ATTTTAATCATCCAGAGTCTCTCTCATCCCAACATTGTGAAACTGCATGAGGTCTACGAA  
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ATCGTTGAAAATGTGAAGTTTCCAGAGCCCGAGGCTGCAGTTATGATCACAGACTTGTGT  
AAGGCCTTCGTCCACATGCACGACAAGAATATCGTCCACCGGGACGTGAAACCAGAAAAC  
CTCCTGGTTTCAGCGAAATGAAGACAAGTCTATCACCTTGAAGCTGGCTGATTTTGGCTTG  
GCCAAATATGTGGTGAGGCCTATATTTACTGTGTGTGGGACGCCAACATATGTAGCTCCT  
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CTATACATCCTCTTGTGTGGCTTCCCCCTTTCCGAAGTCTCTGAGAGGGACCAAGACGAG  
CTCTTCAACATCATCCAAGTGGGCCAGTTTGAAGTTCTCTCTCTTACTGGGACAACATT  
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CTCCGCTGCTGTCGCCAGGAGTCACTTCACGAGAAGCCAGGTCAACCCGTCGGCCCTTG  
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ACAGCAACAGATATGTGGAATATTGGTATAATAGCATATATGTTGTTAACTCACACATCA  
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TATTCGGAAGAACTTTTTTCATCAGTTTCACAGCTGSCCAGACTTTATTCAGAGCCTT

## FIGURE 2U

TTAGTAAAAAATCCAGAGAAAAGACCAACAGCAGAGATATGCCTTTCTCATTTCTTGGCTA  
CAGCAGTGGGACTTTGAAAACCTTGTTTCACCCTGAAGAACTTCCAGTTCCTCTCAAACCT  
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CACTTTTTTCTTTGACTCATTGGAATTTGAAATTTTATATCCACTCCAGTGAGAT  
TATGATTTGTAGCTTCATATATGACATGTTTATATTGTAAATGCACCTTTTCCATGGAATA  
ATTTAGGGAAGTGTTTAAATGTTAAATTACTAGTTGCTAGCATGTTATGATTTTCATATCC  
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GTGAAAG

SEQ ID NO: 30\_W44160\_M DRK2\_M

CCAGACGCGGCTGCACTTTTCAAACCTCAACTGTAAGAAGCGTCGGTCAGCGTCTGTGCG  
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GCTAGCATATCATTTCTTGCTGAAATTTGTTTGCAGAGGAAAATATTTAAGTATATGA  
CAAAAAATGTAAATTGTGTTTAAAGAGAACACATGCAACTGAAAGAACTCAAGTTCAGTCA  
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CAGGATAGAAGCCCATCATTAGAGCATAGGCACTTCAGGAATTCCTTGTTGTGAAATTCAG  
TGAGTGAGGAGGTGTGACATGCAGCTATCTTTGGGCTCCTTTTGTGTGTGTTCTGCTGGA  
CACACACATGGGAGTGTTTCAGTGTTGTCCGTGGTCAATATCTATGTTTCAGTCCTGATGG

## FIGURE 2V

GAGGGGGCCTAGGGACTGCTTTGGAGATTTCCCACTGGTGTCCATTTTAAGGTCTGTAATA  
ATGTCATGTTAAGATAACAGATCTCATAAATATGCTACTCTATCAGACTCCGTTGCCAAA  
ACAAATTTAAAGCCTGTGTATTGAAGTGGGTGTTAGTCTAACAACCTGTAAATTCTTGAA  
ATTGTTACTAAAATTCCAAATTCTTTAGATAACTTTAAACTATTTAAATTGAGCATTGCT  
GTCTTTGTTTGATTAAAGGTTGAGTTCCTTTATATCTGTTATTTTAAAGGAAAAGTTGT  
TTGCCTTTTGTATATGTGTGTGCATATGTGTATGTGTACAGGTATATGTATATATGTATT  
GATAGATAAAATACAGCCTTTAAACAACCTC

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ATGATCCCTTTGGAGAAGCCAGGCAGCGGCGGCTCCTCCCCAGGCGCCACCTCAGGCTCG  
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CTGTGCCCCGGGCCGGGAGCTGGGCAGGGGGAAATTTGCAGTGGTGAGAAAATGTATAAAG  
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SEQ ID NO: 32\_AA021445\_H

CGGGGCTGCCGGGGCCGGGACTGGGGGAGCCGGGCCCCGCGGGCCGCCTGCTGCCTCCGCC  
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CAAGGTTGCTATCAAGATCATAGATAAGACCCAGCTGGATGAAGAAAACCTTGAAGAAGAT  
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ACCTGAACTCTTTGAAGGAAAAGAATATGATGGGCCCAAAGTGGACATCTGGAGCCTTGG  
AGTTGTCTCTACGTGCTTGTGTGCGGTGCCCTGCCATTTGATGGAAGCACACTGCAGAA  
TCTGCGGGCCCCGCGTGCTGAGTGGAAAGTTCCGCATCCCATTTTTTATGTCCACAGAATG  
TGAGCATTTGATCCGCCATATGTTGGTGTAGATCCCAATAAGCGCCTCTCCATGGAGCA  
GATCTGCAAGCACAAAGTGGATGAAGCTAGGGGACGCCGATCCCAACTTTGACAGGTTAAT  
AGCTGAATGCCAACAATAAGGAAGAAAGACAGGTGGACCCCTGAATGAGGATGTCTT  
CTTGGCCATGGAGGACATGGGACTGGACAAAGAACAGACACTGCAGTCATTAAGATCAGA



## FIGURE 2W

TGCCTATGATCACTATAGTGCAATCTACAGCCTGCTGTGTGATCGACATAAGAGACATAA  
AACCCTGCGTCTCGGAGCACTTCCTAGCATGCCCCGAGCCCTGGCCTTTC AAGCACCAGT  
CAATATCCAGGCGGAGCAGGCAGGTACTGCTATGAACATCAGCGTTCCCCAGGTGCAGCT  
GATCAACCCAGAGAACCAAATTGTGGAGCCGGATGGGACACTGAATTTGGACAGTGATGA  
GGGTGAAGAGCCTTCCCCTGAAGCATTGGTGCGCTATTTGTCAATGAGGAGGCACACAGT  
GGGTGTGGCTGACCCACGCACGGAAGTTATGGAAGATCTGCAGAAGCTCCTACCTGGCTT  
TCCTGGAGTCAACCCCCAGGCTCCATTCTGCAGGTGGCCCCCTAATGTGAACTTCATGCA  
CAACCTGTTGCCTATGCAAACTTGCAACCAACCGGGCAACTTGAGTACAAGGAGCAGTC  
TCTCCTACAGCCGCCACGCTACAGCTGTTGAATGGAATGGGCCCCCTTGGCCGGAGGGC  
ATCAGATGGAGGAGCCAACATCCAAGTGCATGCCAGCAGCTGCTGAAGCGCCCCACGGGG  
ACCCTCTCCGCTTGTCAACCATGACACCAGCAGTGCCAGCAGTTACCCCTGTGGACGAGGA  
GAGCTCAGACGGGGAGCCAGACCAGGAAGCTGTGCAGAGGTA CTGGCAAATAGGTCCAA  
AAGACATACACTGGCCATGACCAACCCTACAGCTGAGATCCCACCGGACCTACAACGGCA  
GCTAGGACAGCAGCCTTTCGGTTCGCCGGTCTGGCCTCCTCACCTGGTACCTGATCAGCA  
TCGCTCTACCTACAAGGACTCCAACACTCTGCACCTCCCTACGGAGCGTTTCTCCCCTGT  
GCGCCGGTTCTCAGATGGGGCTGCGAGCATCCAGGCCTTCAAAGCTCACCTGGAAAAAAT  
GGGCAACAACAGCAGCATCAAACAGCTGCAGCAGGAGTGTGAGCAGCTGCAGAAGATGTA  
CGGGGGGCAGATTGATGAAAGAACCCTGGAGAAGACCCAGCAGCAGCATATGTTATACCA  
GCAGGAGCAGCACCATCAAATTCTCCAGCAACAAATTCAAGACTCTATCTGTCTCTCTCA  
GCCATCTCCACCTCTTCAGGCTGCATGTGAAAATCAGCCAGCCCTCCTTACCCATCAGCT  
CCAGAGGTTAAGGATTAGCCTTCAAGCCCACCCCCAACCAACCAACCATCTCTT  
CAGGCAGCCCAGTAATAGTCCTCCCCCATGAGCAGTGCCATGATCCAGCCTCACGGGGC  
TGCATCTTCTTCCCAGTTTCAAGGCTTACCTTCCCGCAGTGCAATCTTTCAGCAGCAACC  
TGAGAACTGTTCTCTCTCCTCCCAACGTGGCACTAACCTGCTTGGGTATGCAGCAGCCTGC  
TCAGTCACAGCAGGTCAACCATCCAAGTCCAAGAGCCTGTTGACATGCTCAGCAACATGCC  
AGGCACAGCTGCAGGCTCCAGTGCGCGGCATCTCCATCAGCCCCAGTGCTGGTCAGAT  
GCAGATGCAGCACCGTACCAACCTGATGGCCACCCTCAGCTATGGGCACCGTCCCTTGTC  
CAAGCAGCTGAGTGCTGACAGTGACAGGCTCACAGCTTGAACGTGAATCGGTTCTCCCC  
TGCTAACTACGACCAGGCGCATTACACCCCCATCTGTTTTCGGACCAGTCCCGGGGTTT  
CCCCAGCAGCTACAGCCCTTCAACAGGAGTGGGGTTCTCTCCAACCCAAGCCCTGAAAGT  
CCCTCCACTTGACCAATTCCCCACCTTCCCTCCCAGTGACATCAGCAGCCGCCACACTA  
TACCACGTCCGGCACTACAGCAGGCCCTGCTGTCTCCACGCCGCCAGACTATACAAGACA  
CCAGCAGGTACCCACATCCTTCAAGGACTGCTTCTCCCCGGCATTCTGCTCACCGGCCA  
CTCGGACATCCGGCTGCCCCCAACAGAGTTTGACAGCTCATTAAGGAGCAGCAGCAACA  
ACGGCAGCAGCAGCAGCAACAGCAGCAACAGCAAGAATACCAGGAACTGTTTCAGGCACAT  
GAACCAAGGGGATGCGGGGAGTCTGGCTCCCAGCCTTGGGGGACAGAGCATGACAGAGCG  
CCAGGCTTTATCTTATCAAATGCTGACTCTTATCACCATCACACCAGCCCCCAGCATCT  
GCTACAAATCAGGGCACAAGAATGTGTCTCACAGGCTTCTCACCACCCCCGCCCCACGG  
GTATGCTCACAGCCGGCACTGATGCATTACAGAGAGCATGGAGGAGGACTGCTCGTGTGA  
GGGGGCCAAGGATGGCTTCCAAGACAGTAAGAGTTCAAGTACATTGACCAAAGGTTGCCA  
TGACAGCCCTCTGCTCTTGAGTACCGGTGGACCTGGGGACCCTGAATCTTTGCTAGGAAC  
TGTGAGTCATGCCCAAGAATTGGGGATACATCCCTATGGTCATCAGCCAAC'TGCTGCATT  
CAGTAAAAATAAGGTGCCCAGCAGAGAGCCTGTCATAGGGAACTGCATGGATAGAAGTTC  
TCCAGGACAAGCAGTGGAGCTGCCGGATCACAATGGGCTCGGGTACCCAGCACGCCCTC  
CGTCCATGAGCACACAGGCCCCGGGCCCTCCAGAGACACCACACGATCCAGAACAGCGA  
CGATGCTTATGTACAGCTGGATAACTTGCCAGGAATGAGTCTCGTGGCTGGGAAAGCACT  
TAGCTCTGCCCCGATGTGCGATGCAGTTCTCAGTCAGTCTTCCGCTCATGGGCAGCCAGCA  
GTTTCAGGATGGGGAAAATGAGGAATGTGGGGCAAGCCTGGGAAGTTCATGAGCACCAGCA  
CCTGAGTGATGGCAGCCAGCATTTAAACTCCTCTTGCTATCCATCTACGTGTATTACAGA  
CATCTGCTCAGCTACAAGCACCCCGAAGTCTCCTTCAGCATGGAGCAGGCAGGCGTGTA

## FIGURE 2X

ACAAGAAACAGAGAGTTTTGTGTACAGCTTGGSAATGAAAAGTTGATTGTAAACCCACA  
STATCTAGCAGCGTTGTGCCAAATTGCCCTTGTGTTTCTCTCCACCCAAAATATCACAGC  
TGCTTTCTCTCACATTTGTTTCATCCGTGTGCTGTTCTTTTGGGTTCTGAGAGGGTTTTC  
CATGTTTGCTTGTATGACCAAGTCACCAAGGAAATAAACAGGAAGGAAATCCATGTTCTC  
C

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CTGGGCGCGCTGCCGGTCAGGTCGGCCCGCCCTGACAGCTCCGGGAGCCTCAAGCGCGACA  
GGGCGCCCTCACCTCGGGACATCCACACACCGACCGCTCCTGCTCCAGAGGCAACAACCC  
AGCGCGCCTAGCCTGGCGCCGTGCAGCGAAGCCCAAGAGCTGGCCTCGCCACGAAGGTTG  
AACCAGCCAAATTTTCGAGACAGCTCACGGCTTAGAGGAAGGTTTCATCTAAATAAAGGCC  
GGCTAAAGTGACATTGCAGGGATTAAATCCTTCTTTGGCTGCCTGTGTGACCAGAAGGCT  
TATTTGCAAGTTTCTTCTTTCTGCGGTCCAGATTATTAGGTCTCCAGCGCCCTGCAGCT  
TGACAGAAAGAGAAGCATGAAATGAAGGTCAGAGATGAGATCCCGCAGCAGGGACGTGGG  
GGCCTCCCAGGGGCATTTACGCACCAGAGTGCAAGATTCTCTGGCCATCAAGGGAAATAG  
CAAACAGAAGCCTTTGTCTGGGGCACAGCCACCTACCACAAAGCATCAGACTCCACGTC  
TGGCCAGAAAGTTCTTGGAGTCCCATCAGGCCAGTGGGTATGTAACATGTGCCTAATTGT  
ACAGCTAGAGCCTGCAAGTTCAACGTGAGGGAAGGTGGGAAATGTCTTGAGTGAGGCGAG  
CAGCTCCTGGCTGGGCTGGGCAGACTCAGCTACCACGTTCACTGCCTTCTCTCACTAAA  
GCCGAGAGGGAGGCTGCTCAGCTCTCAGGAAAACCTCTTTTGAACCCTGGGCACCTGCTGT  
CCTCAGTTGGCATCTCCCACCTCTGAGCCTCTTCTGCTCCTGCACAACCTGCCTCTTCG  
CTGAGATGGAGACGTGAGCCCCCGTGGACGATGACTGCAGTGTATATGAATGGAGGTGGC  
CTGGTGAACCCCCACTATGCCCGGTGGGATCGGCGCGACAGTGTAGAAAGTGGCTGTCAG  
ACCGAGAGTAGCAAGGAGGGTGAGGAGGGACAGCCCCGCCAGCTGACGCCCTTCGAGAAA  
CTGACACAGGACATGTCCCAGGATGAGAAGGTGGTGAGGGAGATCACGCTGGGGAAACGG  
ATAGGCTTCTACCGAATTCGAGGGGAAATCGGAAGTGGAACCTTCTCCCAAGTGAAGCTT  
GGGATTCACTCCCTAACCAAGAAAAGGTGGCCATTAAGATCCTGGACAAGACCAAGTTA  
GACCAGAAAACCCAGAGGCTACTATCCCGAGAAATCTCCAGCATGGAAAAGCTGCACCAT  
CCCAACATCATCCGCCTTTACGAAGTGGTGGAGACCCTATCCAAGCTGCCTTGGTGATG  
GAGTATGCAGGGGGTGGGGAGCTCTTCGGAATAATTAGCACTGAGGGGAAGCTCTCTGAA  
CCAGAAAGCAAGCTCATCTTCTCCAGATTGTGTCTGCCGTGAAGCACATGCATGAAAAC  
CAAATTATTATAGAGATCTGAAAGCAGAAAATGTATTCTATACCAGTAATACTTGTGTG  
AAGGTGGGCGATTTTGGATTACGACAGTAAGCAAAAAAGGTGAAATGCTGAACACTTTC  
TGTGGGTCTCCTCCCTACGCTGCGCCTGAACTCTTCCGGGACGAGCACTACATCGGCATT  
TACGTGGATATCTGGGCCTTGGGGGTGCTTTTGTACTTCATGGTGACTGGCACCATGCCA  
TTTCGGGCAGAAACCGTGGCCAACTAAAAAAGAGCATCCTCGAGGGCACATACAGTGTA  
CCGCCGCACGTGTCAGAGCCCTGCCACCGACTCATCCGAGGAGTCCTTCAGCAGATCCCC  
ACGGAGAGGTACGGAATCGACTGCATCATGAATGATGAATGGATGCAAGGGGTGCCATAC  
CCTACACCTTTGGAACCTTTCCAACCTGGATCCCAAACATTTGTGCGAAACCAGCACTCTC  
AAGGAAGAAGAAAATGAGGTCAAAGCACTTTAGAACATTTGGGCATTACAGAAGAGCAT  
ATTGCAAATAACCAAGGGAGAGATGCTCGCAGCTCAATCACAGGGGTCTATAGAATTATT  
TTACATAGAGTCCAAAGGAAGAAGGCTTTGGAAAGTGTCCCAGTCATGATGCTACCAGAC  
CCTAAAGAAAGAGACCTCAAAAAAGGGTCCCGTGTCTACAGAGGGGATAAGACACACATCC  
AAATTTTGCTCGATTTTATAAATTGCACTAGACTGCTTGTAACCTAACCAAGATGATTGTT  
GCTGCTTCTAAATTTTTTTCAAGGACAACTTGAGTGGAGACATTTTTGTAATTTTTAAAT  
AAACTTAAATTTGAGATATGCAAAAAA

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ATGTCCACTAGGACCCCATTTGCCAACGGTGAATGAACGAGACACTGAAAACCACACGTCA  
CATGGAGATGGGCGTCAAGAAGTTACCTCTCGTACCAGCCGCTCAGGAGCTCGGTGTAGA

## FIGURE 2Y

AACCTCTATAGCCTCCTGTGCAGATGAACAACCTCACATCGGAACTACAGACTGTTGAAA  
ACAATCGGCAAGGGGAATTTTGCAAAAGTAAAATTGGCAAGACATATCCTTACAGGCAGA  
GAGGTTGCAATAAAAAATAATTGACAAAACCTCAGTTGAATCCAACAAGTCTACAAAAGCTC  
TTCAGAGAAGTAAGAATAATGAAGATTTTAAATCATCCCAATATAGTGAAGTTATTGAA  
GTCATTGAAACTGAAAAAACCTCTACCTAATCATGGAATATGCAAGTGGAGGTGAAGTA  
TTTGACTATTTGGTTGCACATGGCAGGATGAAGGAAAAAGAAGCAAGATCTAAATTTAGA  
CAGATTGTGTCTGCAGTTCAATACTGCCATCAGAAACGGATCGTACATCGAGACCTCAAG  
GCTGAAAATCTATTGTTAGATGCCGATATGAACATTAAAATAGCAGATTTTCGGTTTTAGC  
AATGAATTTACTGTTGGCGGTAAACTCGACACGTTTTGTGGCAGTCTCCATACGCAGCA  
CCTGAGCTCTTCCAGGGCAAGAAATATGACGGGGCCAGAAGTGGATGTGTGGAGTCTGGGG  
GTCATTTTATACACACTAGTCAGTGGCTCACTTCCCTTTGATGGGCAAAACCTAAAGGAA  
CTGAGAGAGAGAGTATTAAGAGGGGAAATACAGAATTCCTTCTACATGTCTACAGACTGT  
GAAAACCTTCTCAAACGTTTCTGGTGCTAAATCCAATTAAACGCGGCACTCTAGAGCAA  
ATCATGAAGGACAGGTGGATCAATGCAGGGCATGAAGAAGATGAACTCAAACCATTTGTT  
GAACCAGAGCTAGACATCTCAGACCAAAAAAGAATAGATATTATGGTGGGAATGGGATAT  
TCACAAGAAGAAATTCAAGAATCTCTTAGTAAGATGAAATACGATGAAATCACAGCTACA  
TATTTGTTATTGGGGAGAAAATCTTCAGAGCTGGATGCTAGTGATTCCAGTTCTAGCAGC  
AATCTTTCACCTGCTAAGGTTAGGCCGAGCAGTGATCTCAACAACAGTACTGGCCAGTCT  
CCTCACCACAAAGTGACAGAGAAGTGTTTCTTCAAGCCAAAAGCAAAGACGCTACAGTGAC  
CATGCTGGACCAGCTATTCCTTCTGTTGTGGCGTATCCGAAAAGGAGTCAGACAAGCACT  
GCAGATGGTGACCTCAAAGAAGATGGAATTTCTCCCGGAAATCAAGTGGCAGTGCTGTT  
GGAGGAAAGGGAATTGCTCCAGCCAGTCCCATGCTTGGGAATGCAAGTAATCCTAATAAG  
GCGGATATTCCTGAACGCAAGAAAAGCTCCACTGTCCCTAGTAGTAACACAGCATCTGGT  
GGAATGACACGACGAAATACTTATGTTTGCAGTGAGAGAACTACAGCTGATAGACACTCA  
GTGATTCAGAATGGCAAAGAAAAACAGCACTATTCCTGATCAGAGAACTCCAGTTGCTTCA  
ACACACAGTATCAGTAGTGACGCCACCCAGATCGAATCCGCTTCCCAAGAGGCACTGCC  
AGTCGTAGCACTTTCCACGGCCAGCCCCGGGAACGGCGAACCAGCAACATATAATGGCCCT  
CCTGCCTCTCCAGCCTGTCCCATGAAGCCACACCATTGTCCCAGACTCGAAGCCGAGGC  
TCCACTAATCTCTTTAGTAAATTAACCTTCAAACTCACAAGGAGTCGCAATGTATCTGCT  
GAGCAAAAAGATGAAAACAAAGAAGCAAAGCCTCGATCCCTACGCTTCACCTGGAGCATG  
AAAACCACTAGTTCAATGGATCCCGGGGACATGATGCGGGAAATCCGCAAAGTGTTGGAC  
GCCAATAACTGCGACTATGAGCAGAGGGAGCGCTTCTTGCTCTTCTGCGTCCACGGAGAT  
GGGCACGCGGAGAACCTCGTGCAGTGGGAAATGGAAGTGTCAGCTGCCAAGACTGTCT  
CTGAACGGGGTCCGGTTTAAGCGGATATCGGGGACATCCATAGCCTTCAAAAATATTGCT  
TCCAAAATTGCCAATGAGCTAAAGCTGTAA

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AAAGGGCCGTCCTGGTCCAGCCGTTCCCTGGGTGCCCCTTGCCGGAACCTCTATCGCTTCC  
TGCCCTGAGGAACAACCCCATGTGGGCAACTATAGGCTGCTAAGGACCATCGGGAAGGGC  
AACTTCGCCAAAGTCAAGCTGGCTCGGCATATCCTCACGGGCGGGGAGGTGCTATTAAG  
ATCATTGATAAGACCCAGCTGAACCCCAAGTAGCTTGACAGAGCTGTTTCAAGAGTCCGA  
ATTATGAAGGGACTCAACCACCCCAACATCGTGAAGCTTTTGAAGGTGATAGAGACGGAG  
AAGACGCTATACCTGGTGATGGAATACGCTAGCGCAGGAGAAGTGTTGACTACCTCGTG  
TCGCACGGCCGCATGAAGGAGAAGGAGGCTCGAGCCAAGTTCCGGCAGATCGTGTACGCC  
GTGCACTACTGTATCAGAAGAACATTGTACACAGGGATCTAAAGGCTGAAAACCTGTTG  
CTGGATGCCGAGGCCAACATCAAAATCGCCGACTTCGGCTTCAGCAATGAGTTCACGCTG  
GGCTCCAAGCTGGACACCTTCTGTGGGAGCCCCCATACGCCGCCCCAGAGCTGTTCCAG  
GGCAAGAAGTATGATGGGCCAGAGGTGGACATCTGGAGCCTGGGTGTCATCCTGTACACG  
CTGGTCAGCGGCTCCCTGCCCTTCGATGGGCACAACCTCAAGGAGCTGCGGGAGCGAGTC  
CTCAGAGGAAAGTACCGGGTCCCTTCTACATGTCTACAGACTGCGAGAGCATTTCTGCGG

## FIGURE 27

AGATTTCTGGTGCTGAACCCCGCAAAACGCTGTACTCTGGAGCAAATCATGAAAGACAAA  
TGGATCAACATCGGCTATGAGGGTGAGGAGCTGAAGCCAGACACGGAGCTCAAAGAGAG  
CGGATGCCGGGTCGGAAAGCGAGCTGCAGTGCAGTGGGCAGTGGAAAGTCGAGGCTTGCCC  
CCCTCCAGCCCCATGGTCAGCAGTGGCCACAACCCCAATAAGGCAGAGATCCCTGAGCGG  
CGGAAGGACAGCACTAGCACCCCTAACAACTCCCCCCCCAGCATGATGACCCGAAGAAAC  
ACCTATGTGTGCACAGAGCGACCAAGGATCTGAACGCCCGTCCTTGTGTGCCAAATGGCAA  
GAAAATAGCTCCGGTACCTCGCGGGTGCCCCCTGCCTCGCCTTCCAGTCATAGCCTGGCT  
CCCCCGTCAGGCGAGCGGAGCCGCTGGCTCGGGGCTCCACCATCCGCAGCACCTTCCAT  
GGGGGCCAGGTCCGAGACCGGCGGGCAGGGAGCGGGAGTGGCGGGGGTGTGCAGAAATGGA  
CCCCCAGCCTCACCCACGCTTGCCACGAGGCGGCACCCCTGCCCTCCGGGCGGCCTCGC  
CCCACCACCAACCTCTTCACCAAGCTGACCTCCAAACTGACCCGAAGGGTCACAGACGAA  
CCTGAGAGAATCGGGGACCTGAGGTCAAAAGTTGCCATCTACCTTGGGATAAAACGGAA  
ACCGCCCCCAGGCTGCTCCGATTCCCCTGGAGTGTGAAGCTGACCAGCTCGCGACCTTCC  
TGAGGCCCTGATGGCTGCCCTGCGACAGGCCACA

SEQ ID NO: 36\_406786.5\_H

GTAGCCGGCTTGGCGTGACCGTCGCCTGATCCAGTTGTTAGAGGTGGAAGCTTGGCAGTT  
GGCCTCCCTTCTTCCCATGGAGGTGGGGGCTTAACAGTCTTTGAAGAGGACCAGAGATG  
CCTTTCCAGAGCCTCCCTTGCCAGTGTGACAGAGGGGCCAGCTGCACAGACCACTGC  
TGAGCCCAGCAGGTGCTTTTCTCAGCCACAGACACCTGAGCAGAAGGAATGGGCTTTC  
CAGACTCTGCCAGAGCAGGACGGCGCTCTCTGAAGACAGATGGAGCTCCTATTGTCTATC  
ATCACTGGCTGCCCAGAATATTTGTACAAGTAAACTGCACTGCCCTGCTGCCCTTGAGCA  
CACGGACCCGTCCGAACCGCGGGGAGTGTGTCTGCTGCTCCCTGCTGCGGGGACTGTC  
CTCAGGTGGTCTCTACCTCTGCTTCCGGCCCCCTGTGTGCAACCCTAACAAAGGCCATCTT  
CACGGTGGATGCCAAGACCACAGAGATCCTCGTTGCTAACGACAAAGCTTGCGGGCTCCT  
GGGTACAGCAGCCAGGACCTGATTGGCCAGAAGCTCACGCAGTTCTTTCTGAGGTGAGA  
TTCTGATGTGGTGGAGGCCCTCAGCGAGGAGCACATGGAGGCCGACGGCCACGCTGCGGT  
GGTGTGTTGGCACGGTGGTGGACATCATCACCCGTAGTGGGGAGAAGATTCCAGTGTCTGT  
GTGGATGAAGAGGATGCGGCAGGAGCGCCGCTATGCTGCGTGGTGGTCTTGGAGCCCGT  
GGAGAGGGTCTCGACCTGGGTGCTTTCCAGAGCGATGGCACCATCACGTGATGTGACAG  
TCTCTTTGCTCATCTTCACGGGTACGTGTCTGGGGAGGACGTGGCTGGGCAGCATATCAC  
AGACCTGATCCCTTCTGTGCAGCTCCCTCCTTCTGGCCAGCACATCCCAAAGAATCTCAA  
GATTGAGAGGTCTGTTGGAAGAGCCAGGGACGGTACCACCTTCCCTCTGAGCTTAAAGCT  
GAAATCCCAACCCAGCAGCGAGGAGGCGACCACCGGTGAGGCGGCCCCCTGTGAGCGGCTA  
CCGGGCATCTGTCTGGGTGTTCTGCACCATCAGTGGCCTCATCACCTCCTGCCGGATGG  
GACCATCCACGGCATCAACCACAGCTTCGCGCTGACACTGTTTGGTTACGGAAAGACGGA  
GCTCCTGGGCAAGAATATCACTTTCTGATTCTTGGTTTCTACAGCTACATGGACCTTGC  
GTACAACAGCTCATTACAGCTCCCAGACCTGGCCAGCTGCCTGGACGTGCGCAATGAGAG  
TGGGTGTGGGAGAGAACTTGGACCCGTGGCAGGGCCAGGACCCAGCTGAGGGGGGCCA  
GGATCCAAGGATTAATGTGCTGCTTGCTGGTGGCCACGTTGTGCCCCGAGATGAGATCCG  
GAAGCTGATGGAAGCCAAGACATCTTCACCGGGACTCAGACTGAGCTGATTGCTGGAGG  
CCAGCTCCTTTCTGCTCTCACCTCAGCCTGCTCCAGGGGTGGACAATGTCCCAGAAGG  
AAGCCTGCCAGTGCACGGTGAACAGGCGCTGCCCAAGGACCAGCAAATCACTGCCTTGGG  
GAGAGAGGAACCTGTGGCAATAGAGAGCCCCGGACAGGATCTTCTGGGAGAAAGCAGGTC  
TGAACCAAGTGGATGTGAAGCCATTTGCTTCTGCGAAGATTCTGAAGCTCCAGTCCCAGC  
TGAGGATGGGGGAGTGTGCTGGCATGTGTGGCCTGTGTGAGAAGGCCAGCTAGAGCG  
GATGGGAGTCAGTGGTCCCAGCGGTTACAGACCTTTGGGCTGGGGCTGCCGTGGCCAAGCC  
CCAGGCCAAGGGTCAGCTGGCGGGGGGAGCCTCCTGATGCACTGCCCTTGCTATGGGAG  
TGAATGGGGCTTGTGGTGGCGAAGCCAGGACTTGGCCCCCAGCCCCCTCTGGGATGGCAGG  
CCTCTCGTTTGGGACACCTACTCTAGATGAGCCGTGGCTGGGAGTGGAACGACCCGAGA

## FIGURE 2AA

AGAGCTGCAGACCTGCTTGATTAAGGAGCAGCTGTCCCAGTTGAGCCTTGACAGGAGCCCT  
GGATGTCCCCCACGCCGAACCTCGTTCCGACAGAGTGCCAGGCTGTCAACGCTCCTGTGTCT  
GTCCTGCGATCTGGGAGGCAGAGACCTGTGCGGTGGCTGCACGGGCAGCTCCTCAGCCTC  
CTATGCCTTGGCCACGGACCTCCCTGGGGGCTTGAAGCAGTGGAGGCCAGGAGGTTGA  
TGTGAATTCGTTTTCTTGGAACTCAAGGAACTCTTTTTCAGTGACCAGACAGACCAAAC  
GTCATCAAATTGTTCTGTGCTACGTCTGAACTCAGAGAGACACCCTCTTCTTGGCAGT  
GGGCTCCGATCCAGATGTAGGCAGTCTCCAGGAACAGGGGTCTGTGTCTCTGGATGACAG  
GGAGCTGTTACTACTGACCGGCACCTGTGTTGACCTTGCCAAGGCCGACGGTTCGGGA  
GAGCTGTGTGGGACATGATCCAACAGAACCGCTTGAGGTTTGTGGTGTCTCTGAGCA  
TTATGCAGCAAGCGACAGAGAAAGCCAGGACACGTTCTTCCACGTTGGATGCTGGCCC  
TGAGGACACGTGCCCATCAGCAGAGGAGCCAAGGCTGAACGTCCAGGTCACCTCCACGCC  
CGTGATCGTGATGCGCGGGGCTGCTGGCCTGCAGCGGGAGATCCAGGAGGGTGCCTACTC  
CGGGAGCTGCTACCATCGAGATGGCTTACGGCTGAGTATACAGTTTGAGGTGAGGCGGGT  
GGAGCTCCAGGGCCCCACACCTCTGTTCTGCTGCTGGCTGGTGAAAGACCTCCTCCACAG  
CCAACGCGACTCAGCCGCCAGGACCCGCTGTTCTTGCCAGCCTGCCGGCTCCACCCA  
CTCTACCGCTGCTGAGCTCACCGGACCCAGCCTGGTGGAAGTGCTCAGAGCCAGACCCTG  
GTTTGAGGAGCCCCCAAGGCTGTGGAAGTGAGGGGTTGGCGGCCTGTGAGGGCGAGTA  
CTCCCAAAGTACAGTACCATGAGCCGCTGGGCAGTGGGGCCTTCGGCTTCGTGTGGAC  
TGCTGTGGACAAGGGAAAAACAAGGAGGTGGTGGTGAAGTTTATTAAGAAGGAGAAGGT  
CTTGAGGATTGTTGGATTGAGGATCCCAAAGTTGGGAAAGTTACTTTAGAGATCGCAAT  
TCTATCCAGGGTGGAGCACGCCAATATCATCAAGGTATTGGATATATTTGAAAACCAAGG  
GTTCTTCCAGCTTGTGATGGAGAAGCACGGCTCCGGCCTAGACCTCTTCGCTTTCATCGA  
CCGCCACCCAGGCTGGATGAGCCCCTGGCGAGCTACATCTTCCGACAAGTGAGAGCAGG  
CCAGAGCCGTCTAGTGTGAGCAGTGGGATACCTGCGCTTGAAGGACATCATCCACCGTGA  
CATCAAGGATGAGAACATCGTGATCGCTGAGGACTTCACAATCAAGCTGATAGACTTTGG  
CTCGGCCGCTACTTGGAAAGGGGAAAATTATTTTATACTTTTTGTGGGACCATCGAGTA  
CTGTGCACCGGAAGTTCTCATGGGGAATCCCTACAGAGGGCCGGAGCTGGAGATGTGGTC  
TCTGGGAGTCACTCTGTACACGCTGGTCTTTGAGGAGAACCCCTTCTGTGAGCTGGAGGA  
GACCGTGGAGGCTGCCATACACCCGCCATACCTGGTGTCCAAAGAACTCATGAGCCTTGT  
GTCTGGGCTGCTGCAGCCAGTCCCTGAGAGACGCACCACCTTGGAGAAGCTGGTGACAGA  
CCCGTGGGTAAACACAGCCTGTGAATCTTGCTGACTATACATGGGAAGAGGTGTTTCGAGT  
AAACAAGCCAGAAAGTGGAGTTCTGTCCGCTGCGAGCCTGGAGATGGGGAACAGGAGCCT  
GAGTGATGTGGCCAGGCTCAGGAGCTTTGTGGGGGCCCCGTTCCAGGCGAGGCTCCTAA  
TGGCCAAGGCTGTTTGCATCCCGGGGATCCCGTCTGCTGACCAGCTAAACACCAATTTT  
TTCTGCTTTTCTCCACTTGGTTTGGAAAATCACACAGTTTTTCAGGCTCCATCTGTTTG

SEQ ID NO: 37\_AA544838\_M 406786\_M

CCACGCGTCCGCATCCCTGCTTGATGAGCCCCTGGCGAGTTTCATCTTTTCGACAACCTAG  
TGTCTGCTGTAGGATACCTGCACTCCCAAGGCATCATCCATAGAGACATCAAGGATGAGA  
ACATTGTGATTGCTGAGGACTTCACAATTAAGCTGATAGATTTTGGCTCAGCTGCCTACT  
TAGAGAGGGGCAAACTATTTTATACCTTTTGTGGAACAATCGAATACTGTGCACCTGAGG  
TTCTCATTGGAAATCCCTACAGAGGGCCAGAGCTGGAGATGTGGTCTCTGGGGGTACCCC  
TGACACGCTCATCTTCGAGGAGAATCCCTTCTGTGAGGTGGAGGAGACCATGGAGGCA  
TTATTCATCCCCATTCTGGTTTCCCAAGAACTTATGAGTCTTCTGTCTGGACTGCTGC  
AGCCTTGCCCTGAGCAGCGGACCACTTTGGAGAAGCTGATCAGGGACCCCTGGGTGACAC  
AGCCTGTGAACCTTGCTAGCTATACTTGGGAAGAGGTGTGTAGGACCAACCAGCCAGAAA  
GTGGCCTGCTGTGAGCTGCAAGTCTGGAGATTGGGAGTAGGAGTCCAAGTGAAATGGCTC  
AGAGAGAGGGTCTCTGTGGGCCTCCTGCTCCCAGGGAGACTCGTGGTGACCAGCACTGCT  
TGCATCTTAAGGACCCCTCTTTGCCAGTCAGCTGAGCAAGCTCTCCTGCTCTTTGGTTTG  
GGCAGTTGTATGGATTTAGGGCTTTCTACCTGGAGAAAGGAAGTTGTGAAGGATTGGGA

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## FIGURE 2BB

TGACTTCTGCTTCTAGATTCCCTATGCAAATGCTACAAGAGCCTGCGATGCTAGTTTTCTT  
AGGTTTATGATATAGACTTGTAATTCATGTTTTTTTATAACCTTGAAAATCATTCTAATG  
TTCAGTTATACTGTACTATTAAAGGGCTTTAAGTTGTAAGCCTCAGAAAGACACAAGGAG  
TGTTTAAGTTCTCTATTTTTTGTGTGTTTGTGTTTGTGCTGTAAGTTTTTGAGACAGGATCTC  
ACCATGTAACTTTGGCTGGCCTGGAACCTCAACTATGTAGACCAGGTAGACCTTAACTGA  
CAGATCTGCCTGCGCTTGCCTCCCAAGCATTAGGACTGATGGTGTGTGTGTCACCATGCCCA  
GTTCTTCCTGGTTTTGTGTGTAGGTTTCTTCCCACTGACTTGGTACATGTGACATGTGA  
CAGATGTATGGAGTCTATAGAAGTGGCCAGACAAAAATGGCCAGAATATTTATTTATTTT  
CTTAAAAATTTTCCAAATTAAAGCTACTTAGTTAACAGTTAACTGGCCAGGACTATATG  
AGATAAACTTGGTTTTCTATTTCTTTTTGT

SEQ ID NO: 38\_AA785735\_H

GGCACGAGGCGCGCCTGGCTGGGCCCTGCGGAGGANGGGAAGGAGCGAAGGAGCGAAGGA  
GCAAGCGGAGCGCAGTTCGCCCCAAGCCAAGCCGCGCTGCCAACCTCCCGCCCCGCCGCG  
CTCCTGTCCGCCGTGTCTAGCAGCGGGGCCAGCATGGTTCATGGCGGATGGCCCCGAGGCA  
CTTGACGCGCGGGCCGGTCCGGGTGGGGTTCTACGACATCGAGGGCACGCTGGGCAAGGG  
CAACTTCGCTGTGGTGAAGCTGGGGCGGCACCGGATCACCAAGACGGAGGTGGCAATAAA  
AATAATCGATAAGTCTCAGCTGGATGCAGTGAACCTTGAGAAAATCTACCGAGAAGTACA  
AATAATGAAAATGTTAGACCACCCTCACATAATCAAACCTTTATCAGGTAATGGAGACCAA  
AAGTATGTTGTACCTTGTGACAGAATATGCCAAAAATGGAGAAATTTTTGACTATCTTGC  
TAATCATGGCCGGTTAAATGAGTCTGAAGCCAGGCGAAAATTTCTGGCAAATCCTGTCTGC  
TGTTGATTATTGTTCATGGTTCGGAAGATTGTGCACCGTGACCTCAAAGCTGAAAATCTCCT  
GCTGGATAACAACATGAATATCAAAATAGCAGATTTTCGGTTTTTGAAATTTCTTTAAAG  
TGGTGAAGTCTGGCAACATGGTGTGGCAGCCCCCTTATGCAGCCCCAGAAGTCTTTGA  
AGGGCAGCAGTATGAAGGACCACAGCTGGACATCTGGAGTATGGGAGTTGTTCTTTATGT  
CCTTGTCTGTGGAGCTCTGCCCTTTGATGGACCGACTCTTCCAATTTTGAGGCAGAGGGT  
TCTGGAAGGAAGATTCCGGATTCCGTATTTTCATGTTCAGAAGATTGCGAGCACCTTATCCG  
AAGGATGTTGGTCTAGACCCATCCAAACGGCTAACCATAGCCCCAAATCAAGGAGCATAA  
ATGGATGCTCATAGAAGTTCTGTCCAGAGACCTGTTCTCTATCCACAAGAGCAAGAAAA  
TGAGCCATCCATCGGGGAGTTTAATGAGCAGGTTCTGCGACTGATGCACAGCCTTGGAAAT  
AGATCAGCAGAAARCCATTGAGTCTTTGCAGAACAAGAGCTATAACCACTTTGCTGCCAT  
TTATTTCTTGTGTTGGTGGAGCGCCTGAAATCACATCGGAGCAGTTTCCCAGTGGAGCAGAG  
ACTTGATGGCCGCCAGCGTCGGCCTAGCACCATTTGCTGAGCAAACAGTTGCCAAGGCACA  
GACTGTGGGGCTCCCAGTGACCATGCATTACCGAACATGAGGCTGCTGCGATCTGCCCT  
CCTCCCCCAGGCATCCAACGTGGAGGCCTTTTCATTTCCAGCATCTGGCTGTGAGGCGGA  
AGCTGCATTTCATGGAAGAAGAGTGTGTGGACACTCCAAAGGTCAATGGCTGTCTGCTTGA  
CCCTGTGCCTCCTGTCTGTTGGTGGGAAGGGATGCCAGTCACTGCCCAGCAACATGATGGA  
GACCTCCATTGACGAAGGGCTGGAGACAGAAGGAGAGGCCGAGGAAGACCCCGCTCATGC  
CTTTGAGGCATTTTCAGTCCACACGCAGCGGGCAGAGACGGCACACTCTGTTCAGAAGTGAC  
CAATCAACTGGTCGTGATGCCTGGGGCAGGGAAAATTTCTCCATGAATGACAGCCCCTC  
CCTTGACAGTGTGGACTCTGAGTATGATATGGGGTCTGTTTCAGAGGGACCTGAACTTTCT  
GGAAGACAACCTTCCCTTAAGGACATCATGTTAGCCAATCAGCCTTCACCCCGCATGAC  
ATCTCCCTTCATAAGCCTGAGACCTACCAACCCAGCCATGCAGGCTCTGAGCTCCCAGAA  
ACGAGAGGTCCACAACAGGTCTCCAGTGAGCTTCAGAGAGGGCCGCAGAGCATCAGATAC  
CTCCCTCACCCAGGGAATTGTAGCATTAGACAACATCTTCAGAATCTGGCTAGAACCAA  
AGGAATTCTAGAGTTGAACAAAGTGCASTTGTTGTATGAACAAATAGGACCGGAGGCAGA  
CCCTAACCTGGCGCCGGCGGCTCCTCAGCTCCAGGACCTTGCTAGCAGCTGCCCTCAGGA  
AGAAGTTTCTCAGCAGCAGGAAGCGTCTCCACTCTCCCTGCCAGCGTGCATCCCCAGCT  
GTCCCCACGGCAGAGCCTGGAGACCCAGTACCTGCAGCACAGACTCCAGAAGCCCAGCCT  
TCTGTCAAAGGCCCGAGAACACCTGTCACTTTATTGCAAAGAACCACCGCGGAGCCTTGA

## FIGURE 2CC

GCAGCAGCTGCAGGAACATAGGCTCCAGCAGAAGCGACTCTTTCTTCAGAAGCAGTCTCA  
ACTGCAGGCCTATTTTAAATCAGATGCAGATAGCAGAGAGCTCCTACCCACAGCCAAGTCA  
GCAGCTGCCCCCTTCCCCGCCAGGAGACTCCACCGCCTTCTCAGCAGGCCCCACCGTTTCA  
CCTGACCCAGCCCCCTGAGCCCCGTCTGGAGCCTTCTCAGCAGATGCAATACAGCCC  
TTTCTCAGCCAGTACCAAGAGATGCAGCTTCAGCCCCCTGCCCTCCACTTCCGGTCCCCG  
GGCTGCTCCTCCTCTGCCCACGCAGCTACAGCAGCAGCAGCCGCCACCGCCACCACCCCC  
TCCACCACCACGACAGCCAGGAGCTGCCCCAGCCCCCTTACAGTTCTCCTATCAGACTTG  
TGAGCTGCCAAGCGCTGCTTCCCCTGCGCCAGACTATCCCACTCCCTGTCAGTATCCTGT  
GGATGGAGCCCAGCAGAGCGACCTAACGGGGCCAGACTGTCCCAGAAGCCCAGGACTGCA  
AGAGGCCCCCTCCAGCTACGACCCACTAGCCCTCTCTGAGCTACCTGGACTCTTTGATTG  
TGAAATGCTAGACGCTGTGGATCCACAACACAACGGGTATGTCCTGGTGAATTAGTCTCA  
GCACAGGAATTGAGGTGGGTGAGGTGAAGGAAGAGTGTATGTTCTATTTTTTATTCAGC  
CTTTTAAATTTAAAGCTTATTTTCTTGCCCTCTCCCTAACGGGGAGAAATCGAGCCACCC  
AACTGGAATCAGAGGGTCTGGCTGGGGTGGATGTTGCTTCTCCTGGTTCTGCCCCACCA  
CAAAGTTTTCTGTGGCAAGTGCTGGAACATAGTTGTAGGCTGAGGCAGGAGAATGGCGTG  
AACCCGGGAGGCGGAGCTTGCAGTGAGCCAAGATCGTGCCACTGCACTCCAGCCTGGGCG  
ACTGAGCAAGACTCCACCTCAAAAAAAAAAAAAAAAAAGGACAAGAGCAGTATCATCTGCCTC  
TGTTTTCTAACTGGACAAAGAGATTTTCTTAAAGTTTCTATCATCTCCCTTCTGACAGGT  
TCTACAGTGTGGTCTGAAGCACCTGTAATGTCAGAGCCCTTGTCTGGCCCTTGGTGGCAG  
GTGAACGAAAGCAGTGGAGCCTCTCACCTTCCAGTAGCCTCTCACATTCTTATTTTACCA  
TTTTTGTCTTAATTAAGGTAGCCTAGCTGATTCTAGAAGACAGCCATCCTACGTGCACCC  
CCACCTTGTGTCCACATCTTCTCCAGGCAGGTTTCAACCTATCAGCAGACTCAGGCACAC  
ACTGGGGCACAGATAGAGAACCAGGCGGCAGCAGTGCTCGCAGACCCACCCAGGGAGAGC  
TGTGATGGGTTCTGCCCAGATACTCTGCTCGCCACCCACAAGGGAGCAATAGCTTATAT  
TTGTACATTAGTTTTTACCAAGCACTTTCTCTTCTAACCCCTCACAACAATTCTATGAAATT  
AGCTGGGGAGATACTGTCCTTATTTTTTACAGCTGAAGAAACCAAAGCTTTGGGAAGTTT  
GTGACTTCTCTGAGATCACAGCTGGTGATAGAAGGAGCTGGGACACGCGCTTGGGTTGAC  
TGGCTTCTGGTTTTGGTTCTCTGGCTTCTAGTGCTGGAAGAAGCCCTCTCTTTCCCTTCT  
CTTTCTCAGTAGCATCTGACTCTTTTTCATAAGCAAACAGCTGTATAAACAAAGCCCCCA  
TTTTGGTCAAGCACAGGGTGAATGTGATATTGTTCCCACAACCTTATTCTCCACTCAACA  
GCCGCCTGGCTTTGGGGAAGAGGCCGCCTTCAGGTGACAGTGACAGCTGTCCAGGTGGCCG  
TGCACTGAACCAGGCTGAGGGAGACAAAACCCCGCAGACCCGCCTTTCAGCGTCC  
AGTTAACTGCAGAAGTTTAGGCTCACCTCAAAGATGTCTAGTTTTTCCAAGTTACAATAC  
AGCAGTTTCTACAGAACACCCCTTCTCAATTGCCAAGGGGCCGCATCGCACGGCATC  
AGGCCACCACTGCAGGCCAGCAGATTCCACCCAGGAACGGTCATGAACTCAGCCTTTGT  
CTCAACGAGGGGCGTAACATTTCTTACAGTCAAGCCCCATCAACTAGAAGTGCTTATTA  
CTTTTAGGATTAAAAAAGTAATAACAGACTTTGACTTAATACTCTGTCTTTTCAGAGGCA  
AAGTGGGTGGGTAGAGGGGAGCTTTAAAAATAGAAGTACAAAACAACATCCTGGAAACAT  
ATGACCCAGATGGAATAATGTCACATTCCCAGTGACAGATAATGGGCTGCTGCTGGCTC  
TGTGGTGTCTGTCTGCAGAAGATTTGCTCAGTCAAGGAAATTCAAGTGGTGAGACCTTTC  
CACCATGGGTGGTAAGAGAAACCTGCCTTACCACAAATCTCTGAAGGGGAAAGAAGTGG  
GAGAAAGGTTTTGCTTCACTTCGGGGACTGCAGTTTGAGAAATAAAAGGGATACAGAGATA  
TCTGCACTTTGTAGAAAGGGCAAGATTATTTGCTTATATCTGAAGGGAGGTGGGTGGTTT  
TGCTGGATGTTTTGGTCTGAAAGAGTTACTTTTGATAAAGTTAATCTAATTGTAGTTATAT  
TTTCTGTGTGCTTTTTTTTTAATTACTAAGAAAAAAATTGGTGAGTTCAGTAGCTTTGGTA  
TTATGAGTGCAAATCATAATAGCTCCAATGTGAAAAAAAATCAAAGTATAACTTGTC  
ACTTAATGTTAGAAAATTGCCTAAAATGCAGTGTAATAAATAATCTCTGTACCAAATAGT  
AATTTAAATGGGGTAATTTTCTGCAAGGAAAATGTACTGTTTTTATGTTTTCAACCCCTCT  
TGA

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## FIGURE 2DD

SEQ ID NO: 39\_AA207220\_H

GCTGTGGCTCCCCGTCCCTGGTGCGGGACCTGTGCCCCGCGCTTCAGCCCTCCCCGCAAGC  
CTATTGATTCCCCCTGCCGCCCTTGCTCCACCTCCTGCTCGCCATGGAGTCGCTGGTTTTT  
GCGCGGCGCTCCGGCCCCACTCCCTCGGCCGAGAGCTAGCCCCGGCCGCTGGCGGAAGGG  
CTGATCAAGTCGCCCCAAGCCCCCTAATGAAGAAGCAGGCGGTGAAGCGGCACCAACAAG  
CACAACTGCGGCACCGCTACGAGTTCCCTGGAGACCCTGGGCAAAGGCACCTACGGGAAG  
GTGAAGAAGGCGCGGGAGAGCTCGGGGCGCCTGGTGGCCATCAAGTCAATCCGGAAGGAC  
AAAATCAAAGATGAGCAAGATCTGATGCACATACGGAGGGAGATTGAGATCATGTCATCA  
CTCAACCACCCTCACATCATTGCCATCCATGAAGTGTTTGAGAACAGCAGCAAGATCGTG  
ATCGTCATGGAGTATGCCAGCCGGGGCGACCTTTATGACTACATCAGCGAGCGGCAGCAG  
CTCAGTGAGCGCGAAGCTAGGCATTTCTTCCGGCAGATCGTCTCTGCCGTGCACTATTGC  
CATCAGAACAGAGTTGTCCACCGAGATCTCAAGCTGGAGAACATCCTCTTGATGCCAAT  
GGGAATATCAAGATTGCTGACTTCGGCCTCTCCAACCTCTACCATCAAGGCAAGTTCCTG  
CAGACATTCTGTGGGAGCCCCCTCTATGCCTCGCCAGAGATTGTCAATGGGAAGCCCTAC  
ACAGGCCCAGAGGTGGACAGCTGGTCCCTGGGTGTTCTCCTCTACATCCTGGTGCATGGC  
ACCATGCCCTTTGATGGGCATGACCATAAGATCCTAGTGAAACAGATCAGCAACGGGGCC  
TACCGGGAGCCACCTAAACCCTCTGATTGCCTGNNTGGCCTGATCCGGTGGCTGTTGATG  
GTGAACCCACCCCGCCGGGCCACCTGGAGGATGTGGCCAGTCACTGGTGGGTCAACTGG  
GGCTACGCCACCCGAGTGGGAGAGCAGGAGGCTCCGCATGAGGGTGGGCACCTGGCAGT  
GACTCTGCCCCGCGCCTCCATGGCTGACTGGCTCCGGCGTTCTCCTCCCGCCCCCTCCTGGAG  
AATGGGGCCAAGGTGTGCAGCTTCTTCAAGCAGCATGCACCTGGTGGGGGAAGCACCACC  
CCTGGCCTGGAGCGCCAGCATTGCTCAAGAAGTCCCGCAAGGAGAATGACATGGCCAG  
TCTCTCCACAGTGACACGGCTGATGACACTGCCCATCGCCCTGGCAAGAGCAACCTCAAG  
CTGCCAAAGGGCATTCTCAAGAAGAAGGTGTCAGCCTCTGCAGAAGGGGTACAGGAGGAC  
CCTCCGGAGCTCAGCCCAATCCCTGCGAGCCCAGGGCAGGCTGCCCCCCTGCTCCCCAAG  
AAGGGCATTCTCAAGAAGCCCCGACAGCGCGAGTCTGGCTACTACTCCTCTCCCGAGCCC  
AGTGAATCTGGGGAGCTCTTGAGCGCAGGCGACGTGTTTGTGAGTGGGGATCCCAAGGAG  
CAGAAGCCTCCGCAAGCTTCAGGGCTGCTCCTCCATCGCAAAGGCATCCTCAAACCTCAAT  
GGCAAGTTCTCCCAGACAGCCTTGAGCTCGCGGCCCCCACCACCTTCGGCTCCCTGGAT  
GAACTCGCCCCACCTCGCCCCCTGGCCCCGGGCCAGCCGACCCTCAGGGGCTGTGAGCGAG  
GACAGCATCCTGTCTCTGAGTCCCTTGACCAGCTGGACTTGCCTGAACGGCTCCCAGAG  
CCCCCACTGCGGGGCTGTGTGTCTGTGGACAACCTCACGGGGCTTGAGGAGCCCCCTCA  
GAGGGCCCTGGAAGCTGCCTGAGGCGCTGGCGGCAGGATCCTTTGGGGGACAGCTGCTTT  
TCCCTGACAGACTGCCAGGAGGTGACAGCGACCTACCGACAGGCACTGAGGGTCTGCTCA  
AAGCTCACCTGAGTGGAGTAGGCATTGCCCCAGCCCGGTGAGGCTCTCAGATGCAGCTGG  
TTGCACCCCGAGGGGAGATGCCTTCTCCCCACCTCCCAGGACCTGCATCCCAGCTCAGA  
AGGCTGAGAGGGTTTGCAGTGGAGCCCTGAGCAGGGCTGGATATGGGAAGTAGGCAAATG  
AAATGCGCCAAGGGTTCAGTGTCTGTCTTACAGCCCTGCTGAACGAAGAGGATACTAAAGA  
GAGGGGAACGGGAATGCCCGGACAGAGTCCACATTGCCTGTTTCTGTGTACATGGAGG  
GGCCACAGAGA

SEQ ID NO: 40\_AA426580\_H, MAK\_V\_H

ATGCCGGCGGCGGCGGGGACGGGCTCCTGGGGGAGCCGGCGGCGCCTGGGGGCGGCGGC  
GGCGCGGAGGACGCGGCCAGGCCCCGCGGCGGCCTGCGAGGGAAGTTTCTGCTGCCTGG  
GTGAGCGGCGTGCCCCGCGAGCGGCTCCGCGACTTCCAGCACCACAAGCGCGTGGGCAAC  
TACCTCATCGGCAGCAGGAAGCTGGGCGAGGGCTCCTTTGCCAAGGTGCGCGAGGGGCTG  
CACGTGCTGACCGGGGAGAAGGTGGCCATAAAAGTCATTGATAAGAAGAGAGCCAAAAAG  
GACACCTATGTACCAAAAAACCTGCGGCGAGAGGGTCAGATCCAGCAGATGATCCGCCAC  
CCCAATATCACTCAGCTCCTTGATATTTTAGAAACGGAAAACAGCTACTACCTGGTCATG  
GAGCTGTGCCCTGGGGGCAACCTGATGCACAAGATCTATGAGAAGAAGCGGCTGGAGGAG



## FIGURE 2EE

TCCGAAGCCCCGAGATACATCCGACAGCTCATCTCTGCCGTAGAGCACCTGCACCGGGGCC  
GGGGTGGTCCACAGAGACTTGAAGATAGAGAATTTGCTACTAGATGAAGACAATAATATC  
AAGCTGATTGACTTTGGTTTGAGCAACTGCGCAGGGATCCTGGGTTACTCGGATCCGTTG  
AGCACACAGTGTGGCAGCCCTGCCTACGCTGCACCTGAACTGCTCGCCAGGAAGAAATAC  
GGCCCCAAAATCGATGTCTGGTCCATAGGTGTGAACATGTATGCCATGTTGACCGGGACG  
CTGCCTTTCACGGTGGAGCCTTTCAGCCTGAGGGCTTTGTACCAGAAGATGGTAGACAAA  
GAAATGAACCCCCCTCCCCACTCAGCTCTCCACAGGTGCCATCAGTTTCCTGCGCTCTCTC  
CTGGAACCGGATCCTGTGAAGAGGCCAAATATTAGCAGGCACTGGCGAATCGCTGGCTT  
AATGAGAATTACACGGSCAAAGTGCCTGTAAATGTCACCTATCCCAACAGGATTTCTCTG  
GAAGATCTGAGCCCCGAGCGTCGTGCTGCACATGACCGAGAAGCTGGGTTACAAGAACAGC  
GACGTGATCAACACTGTGCTCTCCAACCGCGCCTGCCACATCCTGGCCATCTACTTCCTC  
TTAAACAAGAACTGGAGCGCTATTTGTACAGGGAAATCTGACATCCAGGACAGCCTCTGC  
TACAAGACCCGGCTCTACCAGATAGAAAAGTACAGGGCCCCCAAGGAGTCTATGAGGCC  
TCTCTGGACACCTGGACACGAGATCTTGAATTCCATGCCGTGCAGGATAAAAAGCCCCAA  
GAACAAGAAAAAAGAGGGGATTTTCTTCATCGACCATCTCCAAGAAGTTGGACAAGAAC  
CTGCCCTCGCACAAACAGCCCTCAGGCTCGCTTATGACACAGATTGAGAACACCAAAGCC  
CTCCTGAAGGACCGGAAGGCCTCCAAGTCCAGCTTCCCCGACAAAGATTCTTTGGCTGC  
CGCAATATTTTCCGCAAACCTCAGATTCCAATTGTGTGGCTTCTTCTCCATGGAGTTC  
ATCCCCGTGCCACCGCCCAGGACCCGAGGATTGTGAAGAAACCGGAGCCCCATCAGCCA  
GGGCCCCGAAGCACTGGCATCCCCCACAAGGAAGACCCCTGATGCTGGACATGGTGGCG  
TCCTTCGAGTCTGTGGATCGCGACGACCACGTAGAAGTGCTGTCTCCCTCTCATCACTAC  
AGGATTCTGAACTCCCCGGTCAGCTTGGCTCGCAGAAATTCAGCGAGAGGACGCTGTCC  
CCGGGTCTGCCATCCGGAAGCATGTGCGCTCTCCATACTCCTTTGCATCCAACTCTGGTC  
TCTTTTGCTCACGAAGATAAGAACAGCCCCCAAAAGAGGAGGGCCTGTGTTGCCACCT  
CCGGTTCACAGCAATGGCCCCATGCAGCCTCTGGGGAGCCCCAATTGTGTGAAAAGCCGA  
GGCCGGTTCCCTATGATGGGCATCGGACAGATGTTAAGGAAGCGCCATCAGAGTCTGCAG  
CCATCTGCAGATAGGCCCTGGAGGCCAGCCTGCCCCCACTGCAGCCCCTAGCCCCTGTG  
AACCTTGCCTTTGACATGGCCGATGGGGTCAAGACCCAGTGCTAA

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ATGGACACAAAGCTGAACATGCTGAACGAGAAGGTGGACCAGCTCCTGCACTTCCAAGAA  
GATGTACAGAGAAGTTGCAGAGCATGTGCCGAGACATGGGCCACCTGGAGCGGGGCCTG  
CACAGGCTGGAGGCCTCCCGGGCACCAGGGCCCGGGCGGGGCTGATGGGGTTCCCCACATT  
GACACCCAGGCTGGGTGGCCCGAGGTCTTGAGCTGGTGAGGGCCATGCAGCAGGATGCG  
GCCAGCACGGTGGCAGGCTGGAGGCCCTCTTCAGGATGGTGGCTGCGGTGGACAGGGCC  
ATCGCTTTGGTGGGGGCCACGTTCCAGAAATCAAAGGTGGCGGATTTCTCATGCAGGGG  
CGTGTGCCCTGGAGGAGAGGCAGCCAGGTGACAGCCCTGAGGAGTGGGTAAAAGAGGAG  
GAGGTCTGTTTCATGCCTCCAGTTCCCCCAGCTCCGGGGGCAGCAGGACAGAGCCTGCAG  
AAGGATAAGGGGGAGCTGTCTGCCGAGCAGGGGATCTGGGCCACATTGATGACGCTGGTG  
ATCATGGTGACAGCGGCAAATAAAGAGCGAGTGGAAGAAGAGGGAGGAAAACCAAAGCAT  
GTGCTGAGCACCAGTGGGGTGCAGTCTGATGCCAGGGAGCCTGGGGAAGAGAGCCAGAAG  
GCGGACGTGCTGGAGGGGACAGCGGAGAGGCTGCCCCCATCAGAGCGTCAGGGCTGGGA  
GCTGACCCCCGCCAGGCACTGGTCTCACCGGGGCCAGGGAGATGGTGTTCTTGCCCCAGCC  
CAGGCATTCCCTGGCCACCTGCCCTGCCCAAAAGGTGGAAGCCAAGGCTCCTGAGACA  
CCCAGCGAGAACCTCAGGACTGGCCTGGAATTGGCTCCAGCACCCGGCAGGGTCAATGTG  
GTCTCCCCGAGCCTGGAGGTTGCACCAGGTGCAGGACAAGGAGCATCGTCCAGCAGGCCT  
GACCCTGAGCCCTTAGAGGAAGGCACGAGGCTGACTCCAGGGCCTGGCCCTCAGTGCCCCA  
GGGCCTCCAGGGCTGCCAGCCAGGCCAGGGCAACCCACAGTGGTGGAGAAACACCTCCA  
AGGGCAGCCCTGCTGAAGGGCGCTGTGGCCCCGGGCTTCTCTCGGAGGGACCTGGTGT  
CCTAGCATCTTCTGCGCCTGCCTAGGGATCTCCATCCACATACAAGAGATGGATACTCT

[illegible]

GGGGAGATGCGCGCTGTTTGAGTGTGCTGGTGGCGGGGCCCACTGACGTGGAGGTGGATTGG  
CTGTGCCGTGGCCGCGCTGCTGCAGCCTGCACTGCTCAAATGCAAGATGCATTTTCGATGGC  
CGCAAATGCAAGCTGCTACTTACATCTGTACATGAGGACGACAGTGGCGTCTACACCTGC  
AAGCTCAGCACGGCCAAAGATGAGCTGACCTGCAGTGCCCGGCTGACCGTGCGGCCCTCG  
TTGGCACCCCTGTTTACACGGCTGCTGGAAGATGTGGAGGTGTTGGAGGGCCGAGCTGC  
CGTTTCGACTGCAAGATCAGTGGCACCCCGCCCCCTGTTGTTACCTGGACTCATTTTGGC  
TGCCCCATGGAGGAGAGTGAGAACTTGCGGCTGCGGCAGGACGGGGGTCTGCACTCACTG  
CACATTGCCCATGTGGGCAGCGAGGACGAGGGGCTCTATGCGGTCAGTGCTGTTAACACC  
CATGGCCAGGCCCACTGCTCAGCCCAGCTGTATGTAGAAGAGCCCCGGACAGCCGCCTCA  
GGCCCCAGCTCGAAGCTGGAGAAGATGCCATCCATTCCCAGGAGCCAGAGCAGGGTGAG  
CTGGAGCGGCTGTCCATTCCCAGCTTCCTGCGGCCACTGCAGGACCTGGAGGTGGGACTG  
GCCAAGGAGGCCATGCTAGAGTGCCAGGTGACCGGCCTGCCCTACCCACCATCAGCTGG  
TTCCACAATGGCCACCGCATCCAGAGCAGCGACGACCGGCGCATGACACAGTACAGGGAT  
GTCCATCGCTTGGTGTTCCCTGCCGTGGGGCCTCAGCACGCCGGTGTCTACAAGAGCGTC  
ATTGCCAACAAGCTGGGCAAAGCTGCCTGCTATGCCACCTGTATGTACAGATGTGGTC  
CCAGGCCCTCCAGATGGCGCCCCGAGGTGGTGGCTGTGACGGGGAGGATGGTCCACTC  
ACATGGAACCCCCCAGGAGTCTGGACATGGCCATCGACCCGGACTCCCTGACGTACACA  
GTGCAGCACCCAGGTGCTGGGCTCGGACCAGTGGACGGCACTGGTCAACAGGCCTGCGGGAG  
CCAGGGTGGGCAGCCACAGGGCTGCGTAAGGGGGTCCAGCACATCTTCCGGGTCTCTAGC  
ACCACTGTCAAGAGCAGCAGCAAGCCCTCACCCCTTCTGAGCCTGTGCAGCTGCTGGAG  
CACGGCCCAACCCTGGAGGAGGCCCTGCCATGCTGGACAAACCAGACATCGTGTATGTG  
GTGGAGGGACAGCCTGCCAGCGTCACCGTCACATTCAACCATGTGGAGGCCAGGTGCTG  
TGGAGGAGCTGCCGAGGGGCCCTCCTAGAGGCACGGGGCCGGTGTGTACGAGCTGAGCCAG  
CCAGATGATGACCAGTACTGTCTTCGGATCTGCCGGGTGAGCCGCCGGGACATGGGGGGC

## FIGURE 2GG

CTCACCTGCACCGCCCCGAAACCGTCACGGCACACAGACCTGCTCGGTACATTGGAGCTG  
GCAGAGGCCCTCGGTTTGGTCCATCATGGAGGACGTGGAGGTGGGGGCTGGGGAACT  
GCTCGCTTTGCGGTGGTGGTTCGAGGGAAAACCACTGCCGGACATCATGTGGTACAAGGAC  
GAGGTGCTGCTGACCGAGAGCAGCCATGTGAGCTTCGTGTACGAGGAGAATGAGTGCTCC  
CTGGTGGTGGTCTCAGCACGGGGGCCAGGATGGAGGCGTCTACACCTGCACCGCCCCAGAAC  
CTGGCGGGTGAGGTCTCCTGCAAAGCAGAGTTGGCTGTGCATTTCAGCTCAGACAGCTATG  
GAGGTGAGGGGGTTCGGGGAGGATGAGGACCATCGAGGAAGGAGACTCAGCGACTTTTAT  
GACATCCACCAGGAGATCGGCAGGGGTGCTTTCTCCTACTTGCGGCGCATAGTGGAGCGT  
AGCTCCGGCCTGGAGTTTGGCGCAAGTTCATCCCCAGCCAGGCCAAGCCAAAGGCATCA  
GCGCGTCGGGAGGCCCGGCTGCTGGCCAGGCTCCAGCACGACTGTGTCTCTACTTCCAT  
GAGGCCTTCGAGAGGCGCCGGGGACTGGTCAATTGTACCGAGCTCTGCACAGAGGAGCTG  
CTGGAGCGAATCGCCAGGAAACCCACCGTGTGTGAGTCTGAGATCCGGGCCTATATGCGG  
CAGGTGCTAGAGGGAATACACTACCTGCACCAGAGCCACGTGCTGCACCTCGATGTCAAG  
CCTGAGAACCTGCTGGTGTGGGATGGTGTGCTGCGGGCGAGCAGCAGGTGCGGATCTGTGAC  
TTTGGGAATGCCCAGGAGCTGACTCCAGGAGAGCCCCAGTACTGCCAGTATGGCACACCT  
GAGTTTGTAGCACCCGAGATTGTCAATCAGAGCCCCGTGTCTGGAGTCACTGACATCTGG  
CCTGTGGGTGTTGTTGCCTTCCTCTGTCTGACAGGAATCTCCCCGTTTGTGGGGAAAT  
GACCGGACAACATTGATGAACATCCGAAACTACAACGTGGCCTTCGAGGAGACCACATTC  
CTGAGCCTGAGCAGGGAGGCCCGGGGCTTCCTCATCAAAGTGTGGTGCAGGACCGGCTG  
AGACCTACCGCAGAAGAGACCCTAGAACATCCTTGTTCAAACCTCAGGCAAAGGGCGCA  
GAGGTGAGCACGGATCACCTGAAGCTATTCCTCTCCCGGCGGAGGTGGCAGCGCTCCAG  
ATCAGCTACAAATGCCACCTGGTGCTGCGCCCCATCCCCGAGCTGCTGCGGGCCCCCCCCA  
GAGCGGGTGTGGGTGACCATGCCCAGAAGGCCACCCCCCAGTGGGGGGCTCTCATCTCC  
TCGGATTCTGAAGAGGAAGAGCTGGAAGAGCTGCCCTCAGTGCCCCGCCCACTGCAGCCC  
GAGTTCTCTGGCTCCCGGTGTCCCTCACAGACATTCCCCTGAGGATGAGGCCCTGGGG  
ACCCCAGAGACTGGGGCTGCCACCCCCATGGACTGGCAGGAGCAGGGAAGGGCTCCCTCT  
CAGGACCAGGAGGCTCCAGCCAGAGGCCCTCCCTCCCCAGGCCAGGAGCCCGCAGCT  
GGGGCTAGCCCCAGGCGGGGAGAGCTCCGCAGGGGCAGCTCGGCTGAGAGCGCCCTGCCC  
CGGGCCGGGCGCGGGAGCTGGGCCGGGGCCTGCACAAGGCGGCGTCTGTGGAGCTGCCG  
CAGCGCCGAGCCCCGGCCGGGAGCCACCCGCTGGCCCGGGGAGGCCCTGGGTGAGGGC  
GAGTATGCCCAGAGGCTGCAGGCCCTGCGCCAGCGGCTGCTGCGGGGAGGCCCCGAGGAT  
GGCAAGGTCAGCGGCCTCAGGGGTCCCTGCTGGAGAGCCTGGGGGGCGGTGCTCGGGAC  
CCCCGGATGGCACGAGCTGCCTCCAGCGAGGCAGCGCCCCACCACAGCCCCCACTCGAG  
AACCAGGGCCTGCAAAAGAGCAGCAGCTTCTCCCAGGGTGAGGCGGAGCCCCGGGGCCGG  
CACCGCCGAGCGGGGGCGCCCTCGAGATCCCCGTGGCCAGGCTTGGGGCCCGTAGGCTA  
CAGGAGTCTCCTTCCCTGTCTGCCCTCAGCGAGGCCAGCCATCCAGCCCTGCACGGCCC  
AGCGCCCCCAAACCCAGTACCCCTAAGTCTGCAGAACCTTCTGCCACCACACCTAGTGAT  
GCTCCGCAGCCCCCGCACCCAGCCTGCCCAAGACAAGGCTCCAGAGCCCAGGCCAGAA  
CCAGTCCGAGCCTCCAAGCCTGCACCACCCCCCAGGCCCTGCAAACCTAGCGCTGCC  
CTCACACCTATGCTCAGATCATTCAGTCCCTCCAGCTGTCAGGCCACGCCCAGGGCCCC  
TCGCAGGGCCCTGCCGCGCCGCTTCAGAGCCCAAGCCCCACGCTGCTGTCTTGGCCAGG  
GTGGCCTCCCCACCTCCGGGAGCCCCGAGAAGCGCGTGGCCTCAGCCGGGGGTCCCCCG  
GTGCTAGCCGAGAAAGCCCCGAGTTCCACGGTGCCCCCAGGCCAGGCAGTCTCAGT  
AGCAGCATCGAAACTTGGAGTCGGAGGCCGTGTTTCGAGGCCAAGTTCAAGCGCAGCCGC  
GAGTCGCCCCCTGTGCTGCGGTGCGGCTGCTGAGCCGTTTCGCGCTCGGAGGAGCGCGGC  
CCCTTCCGTGGGGCCGAGGAGGAGGATGGCATATACCGGCCAGCCGGCGGGGACCCCC  
CTGGAGCTGGTGCAGCGCCTGAGCGCTCACGCTCGGTGCAGGACCTCAGGGCTGTGGGA  
GAGCCTGGCCTCGTCCGCCGCTCTCGCTGTCACTGTCCCAGCGGCTGCGGCGGACCCCT  
CCCGCGCAGCGCCACCCGGCCTGGGAGGCCCGCGGCGGGGACGGAGAGAGCTCGGAGGGC  
GGGAGCTCGGCGCGGGGCTCCCCGGTGCTGGCGATGCGCAGGCGGCTGAGCTTCACCTG

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FIGURE 2HH

GAGCGGCTGTCCAGCCGATTGACAGCGCAGTGGCAGCAGCGAGGACTCGGGGGGGCGCGTCC  
GGCCGCAGCACGCGCGCTGTTCCGACGCGCTTCGACGGGCCACGTCCGAGGGGCGAGASTCTG  
GGCGGCTTTGGCGCTTCCGACACACAGTTGGCGCGCCAGGCCGCGGCCACACGCGCTTCC  
GCGGAGTCCCTGGGCTCCGAGGGCCAGCGCCACGTGGGGCTCCTCAGCCCCAGGGGAAAGC  
CGAAGCCGCGCTCCGCTGGGGCTTCTCTCGGCCGCGGAAGGACAAGGGGTATCGCCACCA  
AACCTCTCTGCCAGCGTCCAGGAGGAGTTGGGTCAACAGTACGTGCGCAGTGAGTCAGAC  
TTCCCCCAGTCTTCCACATCAAACCTCAAGGACCAGGTGCTGCTGGAGGGGGAGGCAGCC  
ACCCTGCTCTGCCTGCCAGCGGCTTGCCTGACCCGCACATCTCCTGGATGAAAGACAAG  
AAGTCTTTGAGGTGAGAGCCCTCAGTGATCATCGTGTCTTGCAAAGATGGGCGGCAGCTG  
CTCAGCATCCCCCGGGCGGGCAAGCGGCACGCCGGTCTCTATGAGTGCTCGGCCACCAAC  
GTACTGGGCAGCATCACCAGCTCCTGTACCGTGGCTGTGGCCCGAGTCCCAGGAAAGCTA  
GCTCCTCCAGAGGTAACCCAGACCTACCAGGACACGGCGCTGGTGCTGTGGAAGCCGGA  
GACAGCCGGGCACCTTGCACGTATACGCTGGAGCGGCGAGTGGATGGGGAGTCTGTGTGG  
CACCTGTGAGCTCAGGCATCCCCGACTGTTACTACAACGTGACCCACCTGCCAGTTGGC  
GTGACTGTGAGGTTCCGTGTGGCCTGTGCCAACCGTGCTGGGCAGGGGGCCCTTCAGCAAC  
TCTTCTGAGAAGGTCTTTGTGAGGGTACTCAAGATTCTTCAGCTGTGCCATCTGCTGCC  
CACCAAGAGGGCCCTGTACCTCAAGGCCAGCCAGGGCCCGGCTCCTGACTCTCCTACC  
TCACTGGCCCCACCCCTAGCTCCTGCTGCCCCACACCCCGCTCAGTCACTGTACGCCCC  
TCATCTCCCCCACACCTCCTAGCCAGGCCTTGTCTCGCTCAAGGCTGTGGGTCCACCA  
CCCCAAACCCCTCCACGAAGACACAGGGGCCTGCAGGCTGCCCGGCCAGCGGAGCCACC  
CTACCCAGTACCCACGTACCCCAAGTGAGCCCAAGCCTTTCGTCTTGACACTGGGACC  
CCGATCCCAGCCTCCACTCCTCAAGGGGTTAAACCAGTGTCTTCTCTACTCCTGTGTAT  
GTGGTGACTTCTTTGTGTCTGCACCAACAGCCCCCTGAGCCCCAGCCCCCTGAGCCCCCT  
CCTGAGCCTACCAAGGTGACTGTGCAGAGCCTCAGCCCGGCCAAGGAGGTGGTCAGCTCC  
CCTGGGAGCAGTCCCCGAAGCTCTCCAGGCCTGAGGGTACCACTCTTCGACAGGGTCCC  
CCTCAGAAACCCCTACACCTTCTTGAGGAGAAAGCCAGGGGGCCGCTTTGGTGTTGTGCGA  
GCGTGCCGGGAGAATGCCACGGGGCGAACGTTCTGTGGCCAAGATCGTGCCCTATGCTGCC  
GAGGGCAAGCCGCGGGTCTGACAGGAGTACGAGGTGCTGCGGACCCTGCACCACGAGCGG  
ATCATGTCCCTGCACGAGGCCTACATCACCCCTCGGTACCTCGTGCTCATTGCTGAGAGC  
TGTGGCAACCGGGAACCTCCTCTGTGGGCTCAGTGACAGGTTCCGGTATTCTGAGGATGAC  
GTGGCCACTTACATGGTGACGCTGCTACAAGGCCTGGACTACCTCCACGGCCACCACGTG  
CTCCACCTAGACATCAAGCCAGACAACCTGCTGCTGGCCCCCTGACAATGCCCTCAAGATT  
GTGGACTTTGGCAGTGCCCAGCCCTACAACCCCCAGGCCCTTAGGCCCCCTTGGCCACCGC  
ACGGGCACGCTGGAGTTTATGGCTCCGGAGATGGTGAAGGGAGAACCATCGGCTCTGCC  
ACGGACATCTGGGGAGCGGGTGTGCTCACTTACATTATGCTCAGTGACGCTCCCCGTTT  
TATGAGCCAGACCCCCAGGAAACGGAGGCTCGGATTGTGGGGGGCCGCTTTGATGCCTTC  
CAGCTGTACCCCAATACATCCCAGAGCGCCACCCTCTTCTTGCGAAAGGTTCTCTCTGTA  
CATCCCTGGAGCCGGCCCTCCCTGCAGGACTGCCTGGCCACCCATGGTTGCAGGACGCC  
TACCTGATGAAGCTGCGCCGCCAGACGCTCACCTTACCACCAACCGGCTCAAGGAGTTC  
CTGGGCGAGCAGCGGCGCGCGGGCTGAGGCTGCCACCCGCCACAAGGTGCTGCTGCGC  
TCCTACCCTGGCGGCCCTTAGAGGCACGGACCACAGCCAGGCCTCGGGCTTCAACTGGGG  
TTCCACCAATGCCACGGGACATTCCAGGGCCACGCTGAGCCAGGCGGGCCTGGGGCTT  
CGGTTACCAACAGCAGCAACATCTGGCTGGGCTCTTACCTCATAGACCTTCAAGGACAGA  
GACCCAGGGCCTGGACCTGATGCCACCCAGGCCAAAGCCAGAGTGGGAGACCCATTGG  
TCAGGCTCAGCAGGGTGGGAACAGGCAGAGGGACAAGAGGGGAATGGAGAAGTGGAGAGG  
AAAAGGAATCGAGGGACAGGAAGGGGGAGGCTCTAGGAAGGTTCTGGGTTGGGGGTCACT  
GCATCTCAGGGAGAACCAAGGAAGGTGGGCATGGCTGGAGAGGAGGAAAAGGAAGGAGCC  
CCAGGTGTCAGGGCAGTAGGCTGGGAGTCACTGTGGCAAAGCGGGGGCAGGACACAGATA  
CAGTGGCAGGGGCCAGGGCTGGGACATGAGAGAAGGCAGCGAGGCGGCAGAGGGAGAAG  
AGAGGACTCAGGTGGAGGTGGGGTGGGTGAGCTGTGAGCATCCCTCAGAGGAGAAATGTS

## FIGURE 2H

GAGAGCTGGAGGCCAGCAGTCACTCACACTCGCTCTGTCTCCTGTCCAGTGGATACAGC  
CCTGGGCGCTCTGCTGGCCCAAGGATGTCCCCACTGCCCCCTCCATGGCCTTTGGCCTTCT  
TCCCATTTCATATTTATTTATTTATTTGACTTTTATGAAGTTTCCCCTTCCATCCGATCCCT  
ACTGCCCATGTTGTCTGACCATCCCTCCCAGCCATCCAGCTGTCTGTCTGTCTGCCACA  
AGGAAATAAAAATGGCAAGCAGCAAAAAA

SEQ ID NO: 43\_AA542015\_M SGK088\_M

GCCACGGACATCTGGGGAGCGGGTGTGCTCACCTACATCATGCTTAGTGGGTACTCCCCA  
TTCTATGAGCCAGACCCCCAGGAAACAGAGGCTCGGATTGTTGGGGTTCGCTTTGATGCC  
TTCCAGTTGTATCCTAACACATCCCAGAGTGCCACCCTCTTCTTGAGAAAGGTCCTCTCA  
GTACATCCCTGGAGCCGGCCCTCTCTGCAGGACTGCTTGGCCCACCCATGGCTGCAAGAT  
GCCTACCTGATGAAGCTGCGCCGCCAGACACTCACCTTCACCACCAACCGGCTCAAGGAA  
TTCCTGGGCGAGCAGCGGCGACGTGCGGCTGAGGCTGCTACCCGTCACAAGGTGCTGCTC  
CGCTCCTACCCTGGCAGCCCCCTAGGTGGCACAGACCCGAGCCCCGCCACGGGCTTCAACT  
TGGGTTCTCACTCGCGCTGCCAAGGGACATTCCAGAGCCCATGCTGAGCTGGACAGGCAG  
GGGCTTCAGATACCAGCAGCAGCAGCAGCAGCAGCAGCAACATCTGGCTGGGCTATT  
ACCTCATGGACCTAAGAGGACAAGGCCCTGGGGCTTCAGCCGAATGTACCCCCGGCCATA  
ACCAGAGCAGGAGACCCACTGGCCAGGCTGGGCAAGGGTGAGAGCAGAAAGAGGCAAGA  
GGGAGTTGGGAAGTGAAGAATGAGACGGAGGATAGAGAGGGAGGAGTTTGAGGAAGGTTT  
TAGGCTGGAGTGGAATGCTATATCTCAGGGAGAAGCCAGAAGGGGACATGGCTGAAGAGG  
AAGAAGGACCCTGTGATGTGGGAATGTGGTGGAGAGGAGGACTGGACATAGAGAGTGTGC  
CAGGAGCCAGAGCAGAGACATAAGGGAGGGCAGAAGGGTAGAAGGCAACAGGAGTGGGCT  
CAGGGGTGGCAGGGCAGGCCAGCAGCTGCATCTTCAGAAAGAGAGAGGAGAAAGGCAAAG  
AGACGAAAGGCCGCTCCAGCTGGTCTCCTGTCCAGCCGATGCAGTTCTGGGCGTTCTCC  
ACTGGCCCAGGGATGTCTCTCACTGCTCCTCCATGGCCTTTGCCCTCCTTCCATTTGTAT  
TTATTTATTTATTGCCTTTTGTGGAGTTTCTTTCTATCCAGTCCCTAGTGCCTATGTTG  
TCCCGACCATCCCCCTTCAGTCACCCAGCTGTCTGTGCAGCTGTCTGTCTGTCTGTCA  
AGGAAAATAAAACAAAACAAAACAAAACAAAACAAAACAAAACAAAACAAAACAGC

SEQ ID NO: 44\_R19772\_H

ATGAAGGGCGGCGACAGGGCTTACACCCGAGGTCCCTCTTTGGGGTGGCTCTTTGCTAAG  
TGCTGCTGTTGCTTCCCGTGTAGAGATGCATACTCTCATTCCTCAAGCGAGAATGGAGGC  
AAGTCCGAGTCCGTAGCCAACCTGCAGGCCAGCCCTCCCTGAACCTTCATCCACAGTTCC  
CCGGGTCCCAAGCGCTCCACCAACACTCTTAAGAAGTGGCTGACGAGTCCCTGTGCGTCGG  
CTCAACAGCGGGAAGGCAGATGGAAACATCAAAAAGCAGAAGAAAGTTTCGCGATGGTCGG  
AAGAGCTTTGACCTGGGATCTCCCAAGCCTGGGGATGAAACAACCCCTCAGGGAGACAGC  
GCTGATGAGAGCAAGAAAGGTTGGGGTGAAGATGAGCCGGATGAAGAGTCACACACACCC  
CTCCCACCACCTATGAAGATTTTTTGACAACGACCTACACAGGATGAAATGTCTCCTCT  
TTGCTAGCAGCCCCGGCAGGCTTCCACTGAAGTACCTACTGCTGCAGACCTTGTCAATGCA  
ATAGAAAAGTTGGTCAAAAACAAGCTGAGTCTAGAAGGAAGCTCATACCGGGGGAGCTTG  
AAAGACCCTGCAGGCTGCCTGAATGAGGGGATGGCCCCACCCACACCTCCTAAAAATCCA  
GAAGAAGAACAGAAAGCCAAGGCCCTGAGAGGCAGGATGTTTGTCTGAATGAGCTGGTA  
CAGACAGAGAAAGACTATGTCAAGGATCTGGGCATTGTGGTGGAGGGCTTCATGAAGAGA  
ATAGAAGAAAAGGGTGTCCCTGAGGATATGCGAGGAAAGGACAAAATCGTGTTTGGAAAT  
ATTCATCAGATTTATGACTGGCATAAGGATTTTTTCTGCGGAACTGGAAAAGTGTATC  
CAGGAGCAAGACAGATTGGCACAGCTCTTTATTAAGCACGAGCGGAAGCTGCACATCTAC  
GTGTGGTATTGTGAGAATAAGCCGCGCTCAGAGTACATCGTTGCTGAGTATGACGCCTAC  
TTTGAGGAGGTAAACAGGAGATAAATCAGAGGCTGACACTGAGTGACTTCCTCATCAAG  
CCCATTTCAGAGAATAACAAAATACCAGTTGCTCCTCAAGGACTTCCTGAGATACAGTGAG  
AAGGCTGGTTTGGAGTGTTTCAGATATCGAGAAAGCAGTGGAGTTAATGTGCCTTGTTCCC

FIGURE 2JJ

AAACGCTGCAATGACATGATGAATCTAGGACGTCTGCAGGGCTTTGAGGGCACTCTGACT  
GCTCAGGGGAAAGCTACTGACGACGACACATTCTATGTGATCGAGCTGGATGCAGGCATG  
CAGTCTCGGACCAAAGAGAGGCGCGTGTTCCTCTTCGAGCAGATTGTCTCTCAGTGAA  
CTGCTCAGGAAGGGATCCCTCACCCCTGGCTACATGTTCAAAAGGAGCATCAAGATGAAT  
TACTTGGTCTTGAGAGGAGAATGTGGACAATGATCCCTGCAAGTTTGCACCTCATGAACAGA  
GAGACTTCTGAGAGGGTTGTTCTGCAAGCCGCCAACGCTGACATCCAGCAGGCCTGGGTG  
CAGGACATCAATCAAGTCTTAGAAACACAGCGAGACTTTTTGAATGCACTGCAATCGCCC  
ATTGAGTATCAACGGAAAGAAAGGAGCACAGCTGTGATGAGGTCTCAACCTGCCAGGCTT  
CCCCAAGCCAGCCCCAGGCCCTACTCCTCTGTTCTGCGGGCTCAGAGAAGCCCCCAAAG  
GGCTCCAGCTATAACCCACCTCTGCCTCCCCTGAAGATATCTACCTCCAATGGCAGTCCA  
GGGTTTGAATACCACCAGCCTGGGGACAAGTTCGAAGCCAGCAAGAACGACCTGGGAGGC  
TGCAATGGGACCTCGTCCATGGCCGTGATCAAAGATTACTATGCACTGAAGGAGAATGAA  
ATCTGTGTGAGCCAAGGTGAGGTGGTCCAGGTCTCGCCGTCAACCAGCAGAACATGTGT  
CTGGTGTACCAGCCTGCCAGCGACCATTCCTCCCGCCGCGAGGGCTGGGTCCCAGGCAGC  
ATCCTGGCGCCCCCTACCAAAGCCACAGCAGCAGAAAGTAGTGACGGGAGCATCAAGAAG  
TCATGTTTATGGCATACTCTACGCATGAGAAAGCGGGCGGAAGTGAGAACACGGGTAAA  
AATGAAGCCACAGGGCCTCGTAAACCCCAAGGATATTCTGGGCAACAAAGTCTCTGTAA  
GAGACGAACAGTTCCGAGGAATCAGAGTGTGATGATCTTGACCCTAATACTAGCATGGAG  
ATCTTAAATCCAAATTTTATCCAAGAAGTGGCCCCAGAATTCCTTGTGCCCTTGGTGGAT  
GTGACCTGCTTGCTTGGGGACACAGTGATACTGCAGTGCAAAGTCTGTGGGCGGCCAAAG  
CCCACCATCACTTGGAAGGGTCCAGACCAGAACATCCTTGACACTGATAACAGCTCAGCC  
ACATACACGGTCTCCTCTTGTGATTCTGGAGAAATCACCTGAAGATCTGTAATCTGATG  
CCCCAAGACAGTGGGATTTATACCTGCATAGCAACAAATGACCACGGGACCACATCAACG  
TCTGCAACAGTCAAAGTGCAAGGTGTTCCAGCAGCCCCCTAACCGCCCCATTGCCAGGAG  
AGAAGCTGCACCTCCGTGATTCTCCGCTGGCTGCCCCCTCCAGCACAGGAAACTGCACT  
ATTTCTGGTTACACTGTGGAGTACAGAGAGGAAGGTTCTCAGATCTGGCAGCAGTCAGTG  
GCTTCGACCTTGGACACTTACCTCGTCATCGAAGACCTTAGTCCCGGGTGTCTTATCAG  
TTCAGAGTCAGTGCCAGTAACCCCTGGGGAATCAGCCTTCCAGCAGGCCCTCGGAGTTT  
GTGCGACTTCCAGAATACGATGCTGCTGCTGATGGTGCCACCATTTCTTGGAAGGAAAAT  
TTTGACTCAGCTTACACTGAGCTGAATGAAATTGGAAGAGGCCGTTTCTCTATAGTAAAG  
AAATGCATTACAAAGCTACCCGCAAAGATGTGGCTGTGAAATTGTGTAACAAAAAATG  
AAGAAGAAAGAACAGGCTGCCCACGAGGCTGCCCTGCTTCAGCACCTACAGCACCCCCAG  
TACATCACTCTCCATGACACCTATGAGTCCCCCACATCCTACATCCTGATCTTGGAAGT  
ATGGATGATGGCCGGCTCTTAGACTACCTTATGAATCATGATGAACTGATGGAGGAAAA  
GTAGCTTTCTATATCCGAGACATCATGGAGGCTCTGCAGTACCTTCACAACTGCAGGGTT  
GCACATTTGGACATAAAGCCTGAAAACCTGCTCATTGACCTACGGATTCCAGTGCCTCGA  
GTGAAGCTCATTGACTTGGAGGATGCTGTCCAGATCTCGGGTCACTTCCACATTACCAC  
CTGCTGGGGAAACCCTGAGTTTGCTGCCCCAGAAGTCATTCAAGGCATCCCCGTCTCCCTG  
GGGACAGACATCTGGAGCATCGGGGTTCTGACATATGTCATGCTGAGTGGGGTCTCCCC  
TTCTTGATGAGAGCAAAGAGGAGACATGTATCAACGTATGCAGGGTGGATTTTACGCTTC  
CCCCATGAATACTTCTGTGGTGTGAGCAATGCTGCCAGAGATTTTATCAATGTGATCTTA  
CAGGAAGATTTTCGGAGGCGGCCACAGCAGCCACATGCTTGACGATCCATGGCTGCAG  
CCCCATAATGGCAGCTACTCTAAGATCCCCCTGGACACCTCCCGCCTAGCATGCTTCATA  
GAACGTCGCAAGCACCAGAATGATGTGCGGCCTATCCCCAATGTCAAGAGCTACATTGTC  
AACCAGGTGAACCAAGGGACGTAG

SEQ ID NO: 45\_5R72\_8\_2\_H

CGCCGCTGTTTGTCTCGCGCGGCCCGTCCACTGCCCTGCGGTTGCTCTGCGGGCTGAA  
AAGTTTCTCCCGGTGCAGAATTCCGGGCTCAGCGACAGCCTGCGCCGAGTGTGCGCACCT  
GTCGGAGACCCGCCAGTCCGCCGGCCCCGGCTTTGTTCTGTCGGAACTGTAGTGGTGAGA

## FIGURE 2KK

AAAAC TCCATGTCTGGGCACGCCTGGCTGATCTTCACCTCTTTCTTCTAGGACCTTCCTC  
TGGGCTGTACGTGTGAATATGTGTCTAGTGCATCCTTAACCTGAGGACTTCACCASTTC  
GAAATTACAGTTTTTACCATCAACTACCTTATCCTTTTTTGGCCTGGTTTTCTTCTCCTCAA  
CAGTGGAACATTTTTTAAAGTTGCTTTTTGTTGCAGAGTTAAACAAATGGCTGATAGTGGC  
TTAGATAAAAAATCCACAAAATGCCCCGACTGTTTCATCTGCTTCTCAGAAAAGATGTACTT  
TGTGTATGTTCCAGCAAAACAAGGGTTCCTCCAGTTTTTGGTGGTGGAAATGTCACAGACA  
TCAAGCATTGGTAGTGCAGAATCTTTAATTTCACTGGAGAGAAAAAAGAAAAAATATC  
AACAGAGATATAACCTCCAGGAAAGATTTGCCCTCAAGAACCTCAAATGTAGAGAGAAAA  
GCATCTCAGCAACAATGGGGTCGGGGCAACTTTACAGAAGGAAAAGTTCTCTACATAAGG  
ATTGAGAATGGAGCTGCTATTGAGGAAATCTATACCTTTGGAAGAATATTGGGAAAAGGG  
AGCTTTGGAATAGTCATTGAAGCGACAGACAAGGAAACAGAAACGAAGTGGGCAATTAAA  
AAAGTGAACAAAGAAAAGGCTGGAAGCTCTGCTGTGAAGTTACTTGAACGAGAGGTGAAC  
ATTCTGAAAAGTGTAACATGAACACATCATACTCTGGAACAAGTATTTGAAACGCCA  
AAGAAAATGTACCTTGTGATGGAGCTTTGTGAGGATGGAGAACTCAAAGAAATTTCTGGAT  
AGGAAAGGGCATTCTCAGAGAATGAGACAAGGTGGATCATTCAAAGTCTCGCATCAGCT  
ATAGCATATCTTCACAATAATGATATTGTACATAGAGATCTGAAACTGGAAAATATAATG  
GTTAAAAGCAGTCTTATTGATGATAACAATGAAATAAACTTAAACATAAAGGTGACTGAT  
TTTGGCTTAGCGGTGAAGAAGCAAAGTAGGAGTGAAGCCATGCTGCAGGCCACATGTGGG  
ACTCCTATCTATATGGCCCCCTGAAGTTATCAGTGCCACGACTATAGCCAGCAGTGTGAC  
ATTTGGAGCATAGGAGTCGTAATGTACATGTTATTACGTGGAGAACCACCTTTTTTGGCA  
AGCTCAGAAGCGAAGCTTTTTGAGTTAATAAGAAAAGGAGAACTACATTTTGAAAATGCA  
GTCTGGAATTCCATAAGTGACTGTGCTAAAAGTGTTTTGAAACAACCTTATGAAAGTAGAT  
CCTGCTCACAGAATCACAGCTAAGGAACTACTAGATAACCAGTGGTTAACAGGCAATAAA  
CTTTCTTCGGTGAGACCAACCAATGTATTAGAGATGATGAAGGAATGGAAAAATAACCCA  
GAAAGTGTTGAGGAAAACACAACAGAAGAGAAGAATAAGCCGTCCACTGAAGAAAAGTTG  
AAAAGTTACCAACCCTGGGGAAATGTCCCTGAGACCAATTACACTTCAGATGAAGAGGAG  
GAAAAACAGTCTACTGCTTATGAAAAGCAATTTCTTGCAACCAGTAAGGACAACCTTTGAT  
ATGTGCAGTTCAGTTTTACATCTAGCAAACCTCCTCCAGCTGAAATCAAGGGAGAAATG  
GAGAAAACCCCTGTGACTCCAAGCCAAGGAACAGCAACCAAGTACCCTGCTAAATCCGGC  
GCCCTGTCCAGAACCAAAAAGAACTCTAAGGTTCCCTCCAGTGTTGGACAGTACAAAAA  
CAAAGCTGCTCTTGTAGCACTTTGATGAGGGGGTAGGAGGGGAAGAAGACAGCCCTATG  
CTGAGCTTGTAGCCTTTTAGCTCCACAGAGCCCCGCCATGTGTTTGCACCAGCTTAAAT  
TGAAGCTGCTTATCTCAAAGCAGCATAAGCTGCACATGGCATTAAGGACAGCCACCAG  
TAGGCTTGGCAGTGGGCTGCAGTGGAAATCAACTCAAGATGTACACGAAGGTTTTTTAGG  
GGGGCAGATACCTTCAATTTAAGGCTGTGGGCACACTTGCTCATTTTTTACTTCAAATTCT  
TATGTTTAGGCACAGCTATTTATAGGGGAAAACAAGAGGCCAAATATAGTAATGGAGGTG  
CCAAATAATTATGTGCACTTTGCACTAGAAGACTTTGTTAGAAAATTACTAATAAACTTG  
CCATACGTATTACAGCAGAAGTGCTTCAGTCATTACATGTGTTTCGTGAGATTTTAGGTT  
GCTATAGATTGTTTAAGACAGCTTATTTTAAATGTAGAAAAATAGGAGATTTTGTAAGTG  
CTTGCCATTAACTTGCTGCTAAATTCCCAATGTATTGATTAAATCAATAAAAAACAGATG  
TTACTC

SEQ ID NO: 46\_SGK309\_H

GGGTCCGCAGCCCGCCCTCACAGGCCCTCCTCACTCCCCTAGGTAGATGGCCCCCTCAGG  
GCAGGCCCGGCGGACACCCCTCCCTCTGGCTGGCGGATGCAGTGCCTAGCGGCCCGCCCTT  
AAGGACGAAACCAACATGAGTGGGGGAGGGGAGCAGGCCGACATCCTGCCGGCCAACTAC  
GTGGTCAAGGATCGCTGGAAGGTGCTGAAAAAGATCGGGGGCGGGGGCTTTGGTGAGATC  
TACGAGGCCATGGACCTGCTGACCAGGGAGAATGTGGCCCTCAAGGTGGAGTCAGCCAG  
CAGCCCAAGCAGGTCCTCAAGATGGAGGTGGCCGTGCTCAAGAAGTTGCAAGGTTCCGGG  
CTCGGGCAGGGGGATGGGAAGGAAGAGATGATGAAGCCAGGGGCTAAGAGAGGGGAAGGAC

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## FIGURE 2LL

CATGTSTGCAGSTTCATTGGCTGTGGCAGGAACGAGAAGTTTAACTATGTAGTGATGCAG  
CTCCAGGGCCCGGAACCTGSCCGACCTGCGCCGTAGCCAGCCGCGAGGCACCTTCACGCTG  
AGCACACATTGCGGCTGCGCAAGCABATCTTGGAGTCCATCGAGGCCATCCACTCTGTG  
GGCTTCCTGCACCGTGACATCAAGCCTTCAAACCTTGGCATGGGCAGGCTGCCCTCCACC  
TACAGGAAGTGCTATATGCTGGACTTCGGGCTGGCCCCGGCAGTACACCAACACCAACGGGG  
GATGTGCGGCCCTCGGAATGTGGCCGGGTTTCGAGGAACGGTTCGCTATGCCTCAGTC  
AATGCCACACAAGAACCGGGAGATGGGCGGCCACGACGACCTGTGGTCCCTCTTCTACATG  
CTGGTGGAGTTTGCAGTGGGCCAGCTGCCCTGGAGGAAGATCAAGGACAAGGAACAGSTA  
GGGATGATCAAGGAGAAGTATGAGCACCGGATGCTGCTGAAGCACATGCCGTCAGAGTTC  
CACCTCTTCTGGACCACATTGCCAGCCTCGACTACTTCACCAAGCCCCGACTACCAGTTG  
ATCATGTGAGTGTGAGAACAGCATGAAGGAGAGGGGCATTGCCGAGAATGAGGCCTTT  
GACTGGGAGAAGGCAGGCACCGATGCCCTCCTGTCCACGAGCACCTCTACCCCCGCCCCCA  
GCAGAACACCCGGCAGACGGCAGCCATGTTTGGGGTGGTCAATGTGACGCCAGTGCCTGG  
GGACCTGCTCCGGGAGAACACCGCGGATGTGCTACAGGGAGAGCACCTGAGTGACCAGGA  
GAATGCACCCCCAATTCTGCCCGGGAGGCCCTCTGAGGGGCTGGGCCACAGTCCCCACCT  
TGTCCCCACCCCGGGGGTCTGAGGCTGAAGTCTGGGAGGAGACAGATGTCAACCGGAA  
CAAACCTCCGGATCAACATCGGCAAAGTAACTGCCGCCAGGGCGAAGGGCGTGGGTGGCCT  
TTTCTCTACCCCCGATTCCAGCCTTGTGCCCTGCCCCTGTTCTCTAAGCACCTGT  
CCCCCGCAATCTCCCTGCTTGCCCGGCCTCTGTTTCCGGTCCCCTCCCCGGCACTAGCC  
TCGCTGTGTCTTCCATCATCATCCTCTGTCTCCTTCACACTGAGGAGACCATCCGCC

SEQ ID NO: 47\_AA234451\_H

GGCGCGCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCGGCGGGCGGCAGGAGGGG  
GAGCAGGTGCTGGCACAAGAGCAGCGGCTTGGGGGAGCCGGCAGCAGCAGTAACAGCAGC  
AGCAGCCGCGCCGCGCCGCGCCAGTAAACGCGGACCGTACCCAGGGGACTACCCAGCCG  
GCCGGCCCTGGAAGCCGCGCTCGGGTCCCGCCGAGTCGGCGGTGGGGGATGGGCAGGCA  
GTGGCGGTCCCGCCTGCCGAGGGTTAACCCCGCCGGTCCCGGTCTTGAGCTGGACCAGA  
GCCCTCCTCCAGAAACCCCTGCGTCCGCCACGGCCAGGTTAAATGGAAACCACCCTTGG  
GAACTGGATGCCTGTGTAGCTGTTCTACCATATCAGTGTATTGCAATGAGTGGGGGAGGA  
GAGCAGCTGGATATCCTGAGTGTGGAATCCTAGTGAAAGAAAGATGGAAAGTGTGAGA  
AAGATTGGGGGTGGGGGCTTTGGAGAAATTTACGATGCCTTGGACATGCTCACCAGGGAA  
AATGTTGCACTGAAGGTGGAATCAGCTCAACAACCAAAACAAGTTCTGAAAATGGAAGTT  
GCTGTTTTGAAAAAGCTGCAAGGGAAAGACCATGTTTGTAGATTTATTGGCTGTGGGAGG  
AATGATCGATTCAACTATGTGGTCATGCAGTTGCAGGGTCCGAATCTGGCAGATCTTCGC  
CGTAGCCAGTCCCGAGGCACATTCACCATTAGTACCACTCTCCGGCTGGGTAGACAGATT  
TTGGAGTCTATTGAAAGCATTCACTCTGTGGGATCTTGNCATCGAGACATCAAACCGTCG  
AACTTCGCTATGGGTGCTTTCTAGTACATGTAGGAAATGTTACATGCTTGATTTTGGC  
TTGGCTCGACAATTTACCAATTCTGTGGTGACGTCAGACCACCTCGAGCTGTGGCAGGT  
TTTCGAGGGACAGTTCGTTATGCATCAATCAACGCACATCGGAACAGGGAAATGGGAAGA  
CATGATGACCTTTGGTCTTATTCTACATGTTGGTGGAGTTTGTGGTTGGTCAGCTGCCC  
TGGAGAAAAATAAAGGACAAGGAGCAAGTAGGCTCTATTAAGGAGAGATATGACCACAGG  
CTCATGTTGAAACATCTCCCTCCAGAATTCAGCATCTTTCTAGACCATATCTCTTCTTTG  
GATTATTTTACAAAACCAGACTACCAGCTTCTTACATCCGTGTTTGACAATAGCATCAAG  
ACTTTTGGAGTAATTGAGAGTGACCCTTTTGAAGTGGGAGAAGACTGGAAATGATGGCTCC  
CTAACAACCACCACTACTTCTACCACCCCTCAGTTGCACACTCGCTTGACCCCTGCTGCA  
ATTGGAATTGCCAATGCTACTCCCATCCCTGGAGACTTGCTTCGAGAAAATACAGATGAG  
GTATTTCCAGATGAACAGCTTAGCGATGGAGAAAATGGCATCCCTGTTGGTGTGTACCA  
GATAAATTGCCTGGATCTCTGGGACACCCCGTCCCCAGGAGAAGGATGTTTGGGAAGAG  
ATGGATGCCAACAAAAACAAGATAAAGCTTGGAAATTGTAAGGCTGCTACTGAAGAGGAG  
AACAGCCATGGCCAGGCAAATGGTCTTCTCAATGCTCCAAGCCTTGGGTACCAATTCGT



## FIGURE 2MM

GTCCGCTCAGAGATTACTCAGCCAGACAGAGATATTCCTACTGGTGCGAAAGTTACGTTCC  
ATTACAGCTTTGAGCTGGAAAAACGTCTGACCCTGGAGCCAAAGCCAGACACTGACAAG  
TTCCTTGAGACCTGGTATAAAATAGTGTATTTTCTTTTTTAAAGCTTCTAAGGTACCAT  
ATTATTGTTGTCATTGTTGTTATTATTATTGTTATATTTCTGTTACATAAAGTCTTTCAAA  
TAAGAAATCCTTGCATTTTTGTAACTGAGTCTATTTCAGCTCCAATTTTTCATCCATGTT  
TTTAATTATTATTATCCTGATTCTTAATTATTATAAATTCTATAGCATATCCTTTGGCTT  
TGGAAGCTGAGCAGTAAGAGCTGATGACTTCCTAACACTAGGTACAAGTTAAATGAACAT  
TTTTACAGTAACCTTTGTTTAGAAAGTAATCTCTTCCACACAACAGTGTAGTGCTGGAGAG  
GGCATGATAAAGATGGCATTAGGCAGAGATGAGGGGAATACATAAAGGAGGGGAAAAAGT  
AATTCATACACAAGGGACGGTGAGTTCAATTCACTTTAGTGAAGACCCTCTAGGAGTAAG  
ATACTGTGGGAAAACAGATACCAATAAGTATATCATGCTTGCCCTAGAGAGTTTGCAATC  
TACCTAGAGAGAAAGGAAGGTGAAACTTGAGAGATCTATATACATAGGTAAAGATTGTAG  
TGCATGGTTTTGAGGCACATTATCCCTACAACAAATTTTGATAACAGAAGAC

SEQ ID NO: 48\_AA435956\_H

ACTTTTACTATATTCTTTGAGATGACTGTTTTTGATTAGAGGGCGAAATCAGCACGTGGT  
GGCTCAAATCTCCTTATGGATAGTGTCTTCTCCTTCCAGCTTTTCATGTTTCAACTTTTG  
CGGGGCCTGGCGTACATCCACCACCAACACGTCTTTCACAGGGACCTGAAACCTCAGAAC  
TACTCATCAGTCACCTGGGAGAGCTCAAACCTGGCTGATTTTGGTCTTGCCCGGGCCAAG  
TCCATTCCCAGCCAGACATACTCTTCAGAAGTCGTGACCCTCTGGTACCGGCCCCCTGAT  
GCTTTGCTGGGAGCCACTGAATATTCTCTGAGCTGGACATATGGGGTGCAGGCTGCATC  
TTTATTGAAATGTTCCAGGGTCAACCTTTGTTTCTGGGGTTTCCAACATCCTTGAACAG  
CTGGAGAAAATCTGGGAGGTGCTGGGAGTCCCTACAGAGGATACTTGGCCGGGAGTCTCC  
AAGCTACCTAACTACAATCCAGAATGGTTCCCACTGCCTACGCCTCGAAGCCTTCATGTT  
GTCTGGAACAGGCTGGGCAGGGTTTCTGAAGCTGAAGACCTGGCCTCCCAGATGCTAAAA  
GGCTTTCCCAGAGACCGCGTCTCCGCCCAGGAAGCACTTGTTTCATGATTATTTTCAGCGCC  
CTGCCATCTCAGCTGTACCAGCTTCTCTGATGAGGAGTCTTTGTTTACAGTTTCAGGAGTG  
AGGCTAAAGCCAGAAATGTGTGACCTTTTGGCCTCCTACCAGAAAGGTCACCAACCCAGCC  
CAGTTTAGCAAATGCTGGTGAAAAGAAAGGGCGAGATCACCAAGGTTCTTCCAGGGCTGT  
ATTTCTGCAGTTTCGGTTTTTCATTTGCTTCAGCTTACTAAGAAGCTTCAAATCTAACTCC  
ATACTGAACAAGGGGCTTTATGTCCTCACCTATGACCTGGAATAGTTTAAATATGGTGT  
CAAGGCAATAGTACATAATAGTGGAAGAAAATTCAGTGGAAGGTTATTGCTATTGTCATT  
TGCATAGAATTTAAGTGATTGATTTAAAAAACTGGACATAAACTAAGTCTAAGAAG

SEQ ID NO: 49\_AA626859\_H

AAATGGAGTTGCTGATGGAGTGATCAAAAGCGTATTATGGCAAACACTTCAAGCTCTTAA  
TTTCTGTATATACATAACTGTATTCACAGAGATATAAAACCTGAAAATATTCTAATAAC  
TAAGCAAGGAATAATCAAGATTTGTGACTTCGGGTTTGACAAATTCTGATTCCAGGAGA  
TGCCTACACCGATTATGTAGCTACGAGATGGTACCGAGCTCCTGAACCTCTTGTTGGGAGA  
TACTCAGTATGGTTCTTCAGTCGATATATGGGCTATTGGTTGTGTTTTTGCAGAGCTCCT  
GACAGGCCAGCCACTGTGGCCTGGAAAATCAGATGTGGACCAACTTTATCTGATAATCAG  
AACACTAGGAAAATTAATCCCAAGACATCAATCAATCTTTAAAAGTAACGGGTTTTTCCA  
TGGCATCAGTATACCTGAGCCAGAAGACATGGAAACTCTTGAGGAAAAGTTCTCAGATGT  
TCATCCTGTGGCTCTGAACTTCATGAAGGGGTGTCTGAAGATGAATCCAGATGACAGATT  
AACCTGTTCCCAACTCCTGGAGAGCTCCTACTTTGATTCTTTTCAAGAGGCCCAAATTAA  
AAGAAAAGCACGTAATGAAGGAAGAAACAGAAGACGCCAACAGAATCAACTGTTGCCTCT  
CATACCAGGAAGCCACATCTCCCCCACACCTGATGGAAGAAAACAAGTCCCTCCAGTTAAA  
ATTTGATCACCTTCCAAACATTTAGGAAAATGTTCTTTCAAGTGCAAAGTAATTTAATAT  
GTACACATTTTGTACAAGTGAGATAGGAATCTCAGTGTTCAAATGCAAATGAGCCATA

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## FIGURE 2NN

TGAAAATTAAGATGCCTTCTAGAATTGGTTTGCTCTGATCATTGCTGATTCCCTTTCCCCA  
TGCTTTTACAT

SEQ ID NO: 50\_AA061797\_M

GAAAATAGCCCTGCGGGAAATCCGTATGCTGAAGTTGAAACACCCAAACCTCGTGAACCT'  
CATCGAGGTGTTT CAGAAGAAAGAGAAAGATGCATCTAGTTTTTGAGTACTGTGATCACAC  
ACTGTTAACGAGCTGGAGAGAAACCCAAACGGAGTTTCTGATGGAGTGATTAAGAGTGT  
GCTATGGCAAACCTTCAAGCCCTTAAGTTCTGTGACAAAGCACAATTGTATTTCATCGGGA  
TGTAACAACTGAAACATCCTAATAACCAAGCAAGGGATGATAAGATTGTGTGACTTTGG  
ATTTGCACGAATTCTAATTCCAGGAGACGCCTACACAGACTATGTTGCCACCAGGTGGTA  
CCGAGCCCCCGAACTTCTCGTGGGAGACACGAAGTACGGTTCCTCTGTAGACGTGTGGGC  
CGTCGGCTGTGTTTTTGCAGAGCTCCTGACGGGTGAGCCACTCTGGCCGGGAAAATCCGA  
CGTGGACCAGCTTTACCTGATCATCAGGACGTTGGGGAAGCTGATTCCAAGACACCAGTC  
TATCTTTAGGAGTAACCAGTTTTTCCGCGGCATCAGCATACTGAACCAGAGGACATGGA  
GACTCTTGAAGAAAAATTCTCAAATGTTGAGCCTGTGGCTTTAAGTTTCATGAAGGGATG  
CCTGAAGATGAATCCTGATGAGAGGCTGACCTGTGCCAGCTGCTGGACAGTGCCTACTT  
TGAGTCTTTTCAAGAGGATCAAATGAAAAGAAAAGCCCGCAGTGAGGGGAGAAGCCGAAG  
GCGCCAGCAGAATCAACTGCTGCCTCTTATTCTGGAAGCCACATCTCCCCACACCTGA  
TGGAAGGAAACAAGTCGTCCAGTTAAAGTTCGATCATCTTCCAAACATTTAGGGGACTCA  
TCCTTCCCAGCACATCCTTTTAATATTGTCTACATAGGAATAAGACGGGAATCCTCAGCA  
TCTCAAATACAGTGAGCGACGTGAACACCAGGGCACCTCTAATCACCACGGGCTCCTCCC  
CTGTGCTTTTTTCCACGCCAGCTCCATCTCCTAAAACATTCTCTTTAAATGTTGCAGTATC  
AAAATGGCACATCCGAAAGAGATGCTTCCAGTTTCACCAGAGCCGGGCTTCCTCAGGCAA  
TCGGTACTGTGCATCTGTGGACTTATGCTCCGACCTAGGGAAAGATTTCACGTAGCCGT  
CTCACTTCAGCCGACCAGTGGTGTCTGAAGCAGACCCAGATCTGCTGGCTGCTGTTTGT  
GGAGGGGATGGCCCTGAGCCCTCTCACTGGAGTTTCTTCTCCGTGCAGCCAGGTCTTACT  
TTAGACTACATTTGTGTTATTGTGGCATGGCAATCGTGAAAGGTGGTCTAGGTTTACCCT  
TGACTCCACAGCAGATGCTAGTCTCCTTCTCGTGAGGAGCTGACAAGTCTGCTTCTAAAA  
CGAACTAGAGAAAAATTCCAAACGTGACCAGTTAGTGGACAGACTACAAGGAATCGACCAC  
CATACCACAGTAACGCCCCCTGGATCCCTGGCTGCCCCACCCACTCTAAGGCTATCCTGGTT  
CACCATGGTTTCTCTTTCTTTTCTTTTCTTTTAAATCTATTTGTACATATGAGAAAGAGGC  
AGAGGGGCGAGAGAAACCTCGTGTGTGAAAATCAAAAGACAAGCAGGAGGCCAGCCTAAG  
CTACATAGCAAGGCCTTTTCTCTACACCCATTCTCTAAGGTTGCTTAAACCCAAGTCCCT  
GCTGCTGATTGTATAAACTATGAATAAGTTCTACATATGTAGGACATATTGTTGTCATTG  
TTGAAATATCTAAGGATCTTGGTAGAAGCAGAAGTGTTCTAAATATTCTCCACACTGGTG  
AGTATCTTGGCATTTTCATTTCTGACCTCATCACAGATGAACACATCAAAGGATGAGTATG  
TATCACTTTGCATCTTAGAATTCTACCTGTTTTAGCTGCGTTAAACCTTGTGAAAGGGCG  
GGGCCATAACTGAACCTGTGGAGTTCTTGCTGTGTGCAGGAAACCCTCTGGTTTTGTCT  
CCAGCATGGAAGAAAACAGCTATAGTCACACCTACCTGAAAGTAGAAATTCAAAGTCACT  
GTCCTTGACTACATATGCAGTCCAAGGCCACGCTGGGCTACACTTCTCCAGGCATGAAGG  
TCCGTGTTTTGTATCAAGGGGAGGAAAGGAGAGTCCAAGGTCAAGGCCAGCCGAGGCTGC  
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CCACCGGCCATTTCTCTAAATATCATTCTGCTGAAAAGGGGGCTTAGTTTAGTTTAGAAT  
GCATTAATGTATGTAGAAGCTGGGCTATTTAGATTATTTGAAATTGTAGCTATTGTTAA  
TTAGCACTTAATACTAAGTACATTATGGTAGTCTAACTATTAGAGTTTACTACAAAG  
AGTTTTTGATTGAATTATATTAAACATATAATATGGATTTTAAAAATTTAAGATGTTTAA  
GAAAGCTATATAAAGATTAAACATTTTTGTGGCTGTATATTTGTGTATATACCTTGGTTG  
TTCTTTAAATTATTTTAAATAAAAGCCAGAAACATT

## FIGURE 200

SEQ ID NO: 51\_AA397553\_H

ATGCCCCAATTTCAGAGAGACATGGGGGCAAGAAGGACGGGAGTGGAGGAGCTTCTGGA  
TTGCAGCCGTCATCGGGAGGCGGCAGCTCTAACAGCAGAGAGCGTCACCGCTTGGTATCG  
AAGCACAAAGCGGCATAAGTCCAAACACTCCAAAGACATGGGGTTGGTGACCCCCGAAGCA  
GCATCCCTGGGCACAGTTATCAAACCTTTGGTGGAGTATGATGATATCAGCTCTGATTCC  
GACACCTTCTCCGATGACATGGCCTTCAAACCTAGACCGAAGGGAGAACGACGAACCTCGT  
GGATCAGATCGGAGCGACCGCCTGCACAAACATCGTCAACCACCAGCACAGGCGTTCCCGG  
GACTTACTAAAAGCTAAACAGACCGAAAAAGAAAAAGCCAAGAAGTCTCCAGCAAGTCG  
GGATCGATGAAGGACCGGATATCGGGAAGTTCAAAGCGTTTGAATGAGGAGACTGATGAC  
TATGGGAAGGCGCAGGTAGCCAAAAGCAGCAGCAAGGAATCCAGGTCATCCAAGCTCCAC  
AAGGAGAAGACCAGGAAAGAACGGGAGCTGAAGTCTGGGCACAAAGACCGGAGTAAAAGT  
CATCGAAAAAGGGAAACACCCAAAAGTTACAAAACAGTGGACAGCCCCAAAACGGAGATCC  
AGGAGCCCCCACAGGAAGTGGTCTGACAGCTCCAAACAAGATGATAGCCCCCTCGGGAGCT  
TCTTATGGCCAAGATTATGACCTTAGTCCCTCACGATCTCATACCTCGAGCAATTATGAC  
TCCTACAAGAAAAGTCTTGAAGTACCTCGAGAAGGCAGTCGGTCAGTCCCCCTTACAAG  
GAGCCTTCGGCCTACCAGTCCAGCACCCCGTCAACGAGCCCCCTACAGTAGGCGACAGAGA  
TCTGTCAAGTCCCTATAGCAGGAGACGGTCGTCCAGCTACGAAAGAAGTGGCTCTTACAGC  
GGGCGATCGCCAGTCCCTATGGTGAAGGCGGTCCAGCAGCCCTTTCTTGAGCAAGCGG  
TCTCTGAGTCGGAGTCCACTCCCCAGTAGGAAATCCATGAAGTCCAGAAGTAGAAGTCCT  
GCATATTCAAGACATTCATCTTCTCATAGTAAAAAGAAGAGATCCAGTTCACGCAGTCGT  
CATTCCAGTATCTCACCTGTCAGGCTTCCACTTAATTCCAGTCTGGGAGCTGAACTCAGT  
AGGAAAAAGAAGGAAAGAGCAGCTGCTGCTGCTGCAGCAAAGATGGATGGAAAGGAGTCC  
AAGGGTTCACCTGTATTTTTGCCTAGAAAAGAGAACAGTTCAGTAGAGGCTAAGGATTCA  
GGTTTGGAGTCTAAAAAGTTACCCAGAAGTGTAAAATTGGAAAAATCTGCCCCAGATACT  
GAACTGGTGAATGTAACACATCTAAACACAGAGGTAAAAAATTCTTCAGATACAGGGAAA  
GTAAAGTTGGATGAGAACTCCGAGAAGCATCTTGTTAAAGATTTGAAAGCACAGGGAACA  
AGAGACTCTAAACCCATAGCACTGAAAGAGGAGATTGTTACTCCAAAGGAGACAGAAACA  
TCAGAAAAGGAGACCCCTCCACCTCTTCCCACAATTGCTTCTCCCCCACCCCTCTACCA  
ACTACTACCCCTCCACCTCAGACACCCCTTTGCCACCTTTGCCTCCAATACCAGCTCTT  
CCACAGCAACCACCTCTGCCTCCTTCTCAGCCAGCATTTAGTCAGGTTCTGTCTCCAGT  
ACTTCAACTTTGCCCCCTTCTACTCACTCAAAGACATCTGCTGTGTCTCTCAGGCAAAT  
TCTCAGCCCCCTGTACAGGTTTCTGTGAAGACTCAAGTATCTGTAACAGCTGCTATTCCA  
CACCTGAAAACCTCAACGTTGCCTCCTTTGCCCTCCACCCCTATTACCTGGAGGTGAT  
GACATGGATAGTCCAAAAGAACTCTTCCTTCAAACCTGTGAAGAAAGAGAAGGAACAG  
AGGACACGTCACCTACTCACAGACCTTCTCTCCCTCCAGAGCTCCCTGGTGGAGATCTG  
TCTCCCCCAGACTCTCCAGAACCAAAGGCAATCACACCACCTCAGCAACCATATAAAAAG  
AGACCAAAAATTTGTTGTCTCGTTATGGAGAAAGAAGACAAACAGAAAGCGACTGGGGG  
AAACGCTGTGTGGACAAAGTTTGACATTATTGGGATTATTGGAGAAGGAACCTATGGCCAA  
GTATATAAAGCCAGGGACAAAGACACAGGAGAACTAGTGGCTCTGAAGAAGGTGAGACTA  
GACAATGAGAAAGAGGGCTTCCCAATCACAGCCATTTCGTGAAATCAAATCCTTCGTCA  
TTAATCCACCGAAGTGTTGTTAACATGAAGGAAATTGTACAGATAAACAAGATGCACTG  
GATTTCAAGAAGGACAAAGGTGCCTTTTACCTTGATTTGAGTATATGGACCATGACTTA  
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AAGTGTCTAACATTTTGTCTGAATAACAGTGGGCAAATCAAACCTAGCAGATTTTGGACTT  
GCTCGGCTCTATAACTCTGAAGAGAGTCGCCCTTACACAAACAAAGTCATTACTTTGTGG  
TACCGACCTCCAGAACTACTGCTAGGAGAGGAACGTTACACACCAGCCATAGATGTTTGG  
AGCTGTGGATGTATTCTTGGGGAATAATTACAAAGAAGCCTATTTTTTCAAGCCAATCTG  
GAACTGGCTCAGCTAGAAGTATCAGCCGACTTTGTGGTAGCCCTTGTCCAGCTGTGTGG  
CCTGATGTTATCAAACCTGCCCTACTTCAACACCATGAAACCGAAGAAGCAATATCGAAGG

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## FIGURE 2PP

CGTCTACGAGAAAGAATTCTCTTTTCATTCCTTCTGCAGCACTTGATTTATTGGACCACATG  
CTGACACTAGATCCTAGTAAGCGGTGCACAGCTGAACAGACCCTACAGAGCGACTTCCTT  
AAAGATGTCGAACTCAGCAAAATGGCTCCTCCAGACCTCCCCCACTGGCAGGATTGCCAT  
GAGTTGTGGAGTAAGAAACGGCGACGTCAGCGACAAAGTGGTGTGTAGTCGAAGAGCCA  
CCTCCATCCAAAACCTTCTCGAAAAGAACTACCTCAGGGACAAGTACTGAGCCTGTGAAG  
AACAGCAGCCCAGCACACCCTCAGCCTGCTCCTGGCAAGGTGGAGTCTGGGGCTGGGGAT  
GCAATAGGCCTTGCTGACATCACACAACAGCTGAATCAAAGTGAATTGGCAGTGTTATTA  
AACCTGCTGCAGAGCCAAACCGACCTGAGCATCCCTCAAATGGCACAGCTGCTTAACATC  
CACTCCAACCCAGAGATGCAGCAGCAGCTGGAAGCCCTGAACCAATCCATCAGTGCCCTG  
ACGGAAGCTACTTCCCAGCAGCAGGACTCAGAGACCATGGCCCCAGAGGAGTCTTTGAAG  
GAAGCACCCCTCTGCCCCAGTGATCCTGCCTTCAGCAGAACAGATGACCCTTGAAGCTTCA  
AGCACACCAGCTGACATGCAGAATATATTGGCAGTTCTCTTGAGTCAGCTGATGAAAACC  
CAAGAGCCAGCAGGCAGTCTGGAGGAAAACAACAGTGACAAGAACAGTGGGCCACAGGGG  
CCCCGAAGAACTCCCACAATGCCACAGGAGGAGGCAGCAGCATGTCCTCCTCACATTCTT  
CCACCAGAGAAGAGGCCCCCTGAGCCCCCGGACCTCCACCGCCGCCACCTCCACCCCCT  
CTGGTTGAAGGCGATCTTTCCAGCGCCCCCAGGAGTTGAACCCAGCCGTGACAGCCGCC  
TTGCTGCAACTTTTATCCCAGCCTGAAGCAGAGCCTCCTGGCCACCTGCCACATGAGCAC  
CAGGCCTTGAGACCAATGGAGTACTCCACCCGACCCCGTCCAAACAGGACTTATGGAAAC  
ACTGATGGGCCTGAAACAGGGTTTCACTGACCATTGACACTGATGAACGAAACTCTGGTCCA  
GCCTTGACAGAATCCTTGGTCCAGACCCTGGTGAAGAACAGGACCTTCTCAGGCTCTCTG  
AGCCACCTTGGGGAGTCCAGCAGTTACCAGGGGCACAGGGTCAGTGCAGTTTCCAGGGGAC  
CAGGACCTCCGTTTTTGCCAGGGTCCCCTTAGCGTTACACCCGGTGGTTCGGGCAACCATT  
CTGAAGGCTGAGGGAAGCAGCAATTCTGTGGTACATGCAGAGACCAAATTGCAAACTAT  
GGGGAGCTGGGGCCAGGAACCACTGGGGCCAGCAGCTCAGGAGCAGGCCTTCACTGGGGG  
GGCCCAACTCAGTCTTCTGCTTATGGAAAACCTCTATCGGGGGCCTACAAGAGTCCCACCA  
AGAGGGGGAAGAGGGAGAGGAGTTCTTTACTAA

SEQ ID NO: 52\_AA789239\_H

TGAAAATGGAGATGTATGAAACCTTGGAAAAGTGGGAGAGGGAAGTTACGGAACAGTCA  
TGAAATGTAAACATAAGAATACTGGGCAGATAGTGGCCATTAAGATATTTTATGAGAGAC  
CAGAACAATCTGTCAACAAAATTGCGATGAGAGAAATAAAGTTTCTAAAGCAATTTTCATC  
ACGAAAACCTGGTCAATCTGATTGAAGTTTTTAGACAGAAAAAGAAAATTCATTTGGTAT  
TTGAATTTATTGACCACACAGTATTAGATGAGTTACAACATTATTGTTCATGGACTAGAGA  
GTAAGCGACTTAGAAAATACCTCTTCCAGATCCTTCGAGCAATTGACTATCTTCACAGTA  
ATAATGTAATCATTCATCGAGATATAAAACCTGAGAATATTTTAGTATCCCAGTCAGGAA  
TTACTAAGCTCTGTGATTTTGGTTTTGCACGAACACTAGCAGCTCCTGGGGACATTTATA  
CGGACTATGTGGCCACACGCTGGTATAGAGCTCCCGAATTAGTATTAAAAGATACTTCTT  
ATGGAAAGTATGTGCCTGTGGATATCTGGGCTTTGGGCTGTATGATCATTGAGATGGCCA  
CTGGAAATCCCTATCTTCTAGTAGTTCTGATTGGATTTACTCCATAAAATTGTTTTGA  
AAGTGNGATTTCATGCCAGAACTGAAAGCTAAATTACTGCAGGAAGCAAAAGTCAATTCAT  
TAATAAAGCCAAAAGAGAGTTCTAAAGAAAATGAACTCAGGAAAGATGAAAGAAAAACAG  
TTTATACCAATACACTGCTAAGTAGTTTCACTTTTGGGAAAGGAAATAGAAAAAGAGAAAA  
AGCCCAAGGAGATCAAAGTCAGAGTTATTAAAGTCAAAGGAGGAAGAGGAGATATCTCAG  
AACCAAAAAAGAAAGAGTATGAAGGTGGACTTGGTCAACAGGATGCAAATGAAAATGTTT  
ATCCTATGTCTCCAGATACAAAACCTTGTAAACATTGAACCACCAAACCTTATCAATCCCA  
GCACTAACTGTAATGGCTTGAAAGAAAATCCACATTGCGGAGGTTCTGTGACAATGCCAC  
CCATCAATCTAACTAACAGTAATTTGATGGCTGCAAATCTCAGTTCAAATCTCTTTTACC  
CCAGTGTGAGGTAACTGAAAGAGCAAAAAAGAGACGCACTTCTTCACAATCTATTGGAC  
AAGTTATGCCTAATAGCAGGCAAGAGGATCCAGGTCCTATTCAAAGCCAAATGGAGAAGG  
GTATATTTAATGAGCGAACAGGTTCACAGTGACCAAATGGCAAATGAGAACAAAAGGAAGC

## FIGURE 2QQ

TGAATTTTTCCAGATCTGACAGGAAAGAATTCCATTTTCCAGAATTGCCTGTCACAATAC  
AGTCAAAAGATACAAAAGGAATGGAAGTTAAACAGATAAAAAATGCTGAAGAGGGAGTCAA  
AGAAAACAGAGTCATCTAAGATACCAACTTTACTTAACGTGGATCAAAATCAAGAAAAAC  
AAGAGTTTATTCCTTATCTCTGCTGTCTGCCTGCTGTCTATTTTCACAAATATTTGCT  
CTCAGCTAACTATCAGGGTGGAGATGGCCATTGCGAGGGGAAGAATTTGAAGAGAAACAG  
GTTTTTTTTCTGGTAGTGTCTTTTCTTTTACATAGTCCAAAAAATACAAGATGACAACTC  
TTCCCGTTTTATTTATCTACAATAGAAGTGTGATGTGAGTTGTTGTTAAGACAGCCATCC  
ATGTGCATGAGCATCATCCAGCTTTTTTTTGTAGCAAAACATTTACTGTTTTCTTTTCCC  
TTTTAAGACTCTGTTGATGTGATAATTTGATTTGGAATTATAAAGTCATCTCTTCTCTGC  
CTTGAA

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CTGGCAGATATAGTTTCATGCTTGTTTACAAATTGATCCTGCTGAGAGGACATCATCTACT  
GATCTTTTGCCTCACGATTACTTTACTAGAGATGGATTTATTGAGAAATTCATACCAGAG  
CTGAGAGCTAAATTATTACAGGAAGCAAAGGTTAATTCATTTATAAAGCCAAAAGAGAAT  
TTTAAAGAAAATGAACCTGTGAGAGATGAGAAGAAATCAGTTTTTACCAACACCCTGCTC  
TATGGAAATCCATCACTTTATGGCAAGGAAGTGGACAGAGACAAAAGGGCCAAGGAGCTC  
AAAGTCAGAGTCATTAAGGCCAAAGGGGGCAAAGGAGATGTCCCAGACCAGAAGAAGCCA  
GAGTATGAAGGCGACCACCGCCAGCAGGGCACAGCTGATGACACACAGCCCTCATCACTG  
GACAAGAAGCCTTCTGTCTTGGAAGTACAAACCCTCTCAATCCCAGTGAGAATTCTGAC  
GGTGTCAAAGAAGACCCACACGCTGGGGGTTGTATGATAATGCCACCTATCAACCTGACA  
AGCAGTAATTTGTTGGCCGCAAATCTCAGTTCAAACCTTTCCCACCCCAATTCACGGTTA  
ACTGAAAGAACAAAAAAGAGACGCACTTCTTCACAACTATTGGACAGACTTTGTCTAAT  
AGCAGACAAGAGGACACAGGTCCACACAAGTCCAAACAGAGAAAGGTGCATTTAATGAG  
CGAACAGGTCAGAATGACCAAAATATCGAGTGGGAACAAAAGAAAGCTGAATTTTCCCAA  
TGCGACAGGAAAGAATTCCATTTCCCTGAACTGCCATTCACAGTGCAGGCGAAGGAGATG  
AAAGGGATGGAAGTTAAACAGATAAAAGTGTGCTGAAGAGAGAATCAAAGAAAACAGATTCA  
TCTAAATACCAACTTTACTTAGTATGGACCCAAATCAAGAAAAACAAGAGGGTGGAGAT  
GGCGATTGTGAGGGGAAGAATTTGAAGAGGAACAGATTTTTTTTTTCCCGATAGTGCTTT  
GTCTTTTAAGTAATCTTAAATAACAAGCTTGACAATTCCTTCCTTTTTATTTTATATAC  
ACTAGAATGTACATAGGTTGCTGCTAAGATAGCCACCCATCCCATCTGCATCAACATCAT  
CTATTTTTTTTGGTTTTGCTAGCAAAATTTTCACAATTTTCTCTATCTTCCAAAACTGT  
TATTTTGATGCTGTGATTGAAATTATAAAGTCACCTCCTCTGTCTGCTTCCTTCCTTGC  
CATGATTACTGAGTGGGTAGTCACATGATGTGCCCTGCTCGCACTGCTCTCAGACTGCTG  
AGACTCAAACCTCATAAGCCAGGGGTCTCCTGGGAAGCACTGGCCTCTTCAAGTGGATGC  
TCGATGAACCTTCTTATCTGTTGTCTTAGTAACCACTCGTTGCCATCACATGATGAAAGA  
CATTCTATTGTCCCCAGTGAAGCATTATAGTACTTACATAACATGTTACAGTGATATGA  
TGTTCCCTAGGTTAACTCCTTGAGATGAACTATTTCTGCACTCTCTGACTCCCCTAGT  
CTAATAGTTCCTTCATTTAGCCAGAAGAATTTCTGAGAAGCGATGCACAACCTGGGA  
AAGGTTTACTTTCTATCCTGGGCTGTTTTCTGTTGCTAAATAATATAGACTGGGTAGTTA  
GTTAACAT

SEQ ID NO: 54\_AA575635\_M CCRK\_M

AGCGCCTCAGGCCAGCTCAAGATAGCTGACTTTGGCCTGGCCCGGGTCTTCTCTCCGGAT  
GGTGGTGCCTCTACACACATCAGGTGGCCACCAGGTGGTACCGAGCTCCTGAACTCCTG  
TATGGCGCTCGGCAGTATGACCAGGGCGTTGACCTATGGGCTGTGGGCTGCATCATGGGA  
GAGCTGTTGAATGGGTCCCCCTGTTCCCGGGCGAAAACGACATTGAACAACCTGTGCTGT  
GTGCTTCGCATCCTGGGTACCCCGAGTCCTCGAGTCTGGCCGGAGATCACAGAGCTGCCT  
GACTACAACAAGATCTCCTTCGAGGAGCAGGCACCAAGTGCCCTGGAGGAGGTGCTGCCT  
GATGCCTCTCCCCAGGCCTTGGACCTGCTGGGCCAGTTCTCCTCTACCCTCCACGACAG

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## FIGURE 2RR

CGTATTGCAGCCTCCCAGGCCCTTCTGCATCAGTACTTCTTCACAGCGCCTCTGCCTGCC  
CATCCATCCGAGCTGCCAATTCTCAGCGCCAGGGGGACCTGCACCCAAGGCTCACCCA  
GGGCCCCCCCCATGTCCACGACTTCCATGTGGATCGACCTATTGAGGAGTCACTGTTGAAC  
CCAGAACTGATTCCGGCCCTTCATCCAGAGGGGTGAGATGCTGGTCCAGGCCTTCTGCT  
CGCCCTAGGAGCACCTCTTTCTGATTTGCCTCCATGGCCTCCCCACGGCTATATATACCA  
CACCTGGTCTGCTCCTGAGTGTGCTTGAGGGCTGGGCTCTGGGAGGCAGAACCGTGAGA  
TGTTTCATCCCAGCAGAGAAAGAGACTCACGTCTACAGACAAAGCCTCCAGAACTGCTA  
GCTGTGTCTTCTCCAGGGCCACCCCTCAGTGGTGCCACCCGGCCTTAGAGATGATTGTC  
AGGCTCTGTCCCCTCTTCAAGGACATTGGTACTACAGCACCACTGGTGGAAGCACAGAG  
TATAAGCTGTCTTCATACTGGGGACACAGCTGGGAAGTCAGACATGTTTTAGTTTTGGTT  
CCACTGGGTGAGGATTTGAGGTTTCATATAAAAGCCCTGGGTGTTTTCTGTCTAATTGCACC  
TTGTCTGTTGCTGTTAGGGAAGGACAATGGTGGGCCTTGATTCACAGGGGTGAGGTA  
CAGAAGGGGCCCTCCTGTGAAGGCCATTTGGGTCTCAGGCTTCCCATGCTATTCACGGGA  
CTTGAGTGCTCATTGGGAGCGAGGGTCCAGAAGCTGAGGCCAGGGATGGACAGTCCAG  
TTCCCGAAGCCCACTTCCCACATGTCGGGTGGGTGAGTCAAGTGAAGCCTGAGGCTGCCTTG  
CAGATGCGGAAGCAGGCATTCTGGAATCCACTCAGTAAATAAATTCCAGTGTGACTCAG

SEQ ID NO: 55\_AA631990\_H

GAACAACAATAACAGAATAAGGAAGAAAATCTCATGATTACCTCAATAAGTACAGAGAAA  
TCTGGTCACACTCACTATCCATTTCATGATTACAACCTCTTCAATACTATCGCGGCCGAGGA  
GGGAAGACGGCAGTTTGGCGACATTTCTCGGCCGAAGGGCCATTTGCTTTTGCGGAGATG  
CGGCATTCCAAAAGAACTCACTGTCTGATTGGGATAGCAGAGAAAGCTGGGGACATGAA  
AGCTATCGTGGAAGTCACAAGCGGAAGAGGAGATCTCATAGTAGCACACAAGAGAACAGG  
CATTGTAAACCACATCACCAGTTTAAAGAATCTGATTGTCATTATTTAGAAGCAAGGTCC  
TTGAATGAGCGAGATTATCGGGACCGGAGATACGTTGACGAATACAGGAATGACTACTGT  
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CATGGTCATGTTTGTATTGTGTTTGAACACTACTGGGACTTAGTACTTACGATTTTCATTAAA  
GAAAACAGCTTTCTGCCATTTCAAATTGACCACATCAGGCAGATGGCGTATCAGATCTGC  
CAGTCAATAAAATTTTTACATCATAATAAATTAACCCATACAGATCTGAAGCCTGAAAAT  
ATTTTGTGTTGTGAAGTCTGACTATGTAGTCAAAATATAATTCTAAAATGAAACGTGATGAA  
CGCACACTGAAAAACACAGATATCAAAGTTGTTGACTTTGGAAGTGCAACGTATGATGAT  
GAACATCACAGTACTTTGGTGTCTACCCGGCACTACAGAGCTCCCGAGGTCAATTTTGGCT  
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CATAACCAGCTAGATTGGGATGAACACAGTTCTGCTGGTAGATATGTTAGGAGACGCTGC  
AAACCGTTGAAGGAATTTATGCTTTGTTCATGATGAAGAACATGAGAACTGTTTGACCTG  
GTTGCAAGAATGTTAGAATATGATCCAACTCAAAGAATTACCTTGGATGAAGCATTGCAG  
CATCCTTTCTTTGACTTATTAATAAAGAAATGAAATGGGAATCAGTGGTCTTACTATATA  
CTTCTCTAGAAGAGATTACTTAAGACTGTGTGAGTCAACTAAACATTCTAATATTTTGT  
AAACATTAAATTATTTTGTACAGTTAAGTGTAATATTGTATGTTTTGTATCAATAGCAT  
AATTAACCTGTTAAGCAAGTATGGTCTTGATAATGCATTAGAAAAATTAAATTAATTTT  
TCTTTTGAATTAACATTTTAAATACCTTTGAAATATCCTTTGTGTCCAGTGATAAAT  
GTGATTGATCTTGCCCTTTGTACATGGAGGTCACTCTGAAGTGATTTTTTTTGTAGTAA  
AGGAAATCTTGACTACTTTATATTCTTAAAGGAATATTCTTTATATACTTCAAATTTAGA

## FIGURE 2SS

ACTTAACTTTAAAAGTTTTTCTTCTGTAATTGTTGAACGGGTGATTATTATTAACTCTAG  
ATAAGCAGGTACTAGAAACCAAACTCAGAAAATGTTTACTGTTAGAATTCTATTAAATT  
TTAAGTGTTGTATTCTTTTTTCATTGGGTGATGTCAGGGTGATAACCAGACATTCATGGAA  
AGGCATGCAGTTTGTCCATTGTGACAGTTTGTTTAATAAAACCATACACACTTTATTT  
AAGATTAATAATCTAACTGGAAAGTCAGCTTGGAAAATGGACATTTCCAAGTATGTTTGGT  
GAGTCACAGATATAAAAATAGAAATTCTGATGAGAGGTTTCAGTTTTTAATACCAAGTCC  
TTAGGAGTCTTAACATTGGCCAGCATCTGTTTATCAAATGACATAAATAACGTAAACCTAT  
AAGAATTAAGTTTATTAATTAGGCAATTTATGTCTGTGATAATTCTTACGGGAGAAAGAG  
GATTTGATTGGAAAGCAGTTTGGGAAGAAAGTGCTGCTGAAATTTCCAGAATTTAATTGA  
TTGGTTACATAAACTTTTTGACTTCAAT

SEQ ID NO: 56\_AA557536\_H

AGTAAGGCCCGCGGGCGTCCTGGCCGCCATGTGCACCGTAGTGGACCCTCGCATTGTCC  
GGAGATACCTACTCAGGCGGCAGCTCGGGCAGGGGAGAACATTCGGGAAATCACGCTCC  
TCCAGGTGAGTGGCCTGGGCCCTCCAGTCCAATCCCCTTGCCCAGGTACAGATCTCTCCA  
GACAGGAGAGAACTGGCCTTCTTGGGCCCCAGAGCACAGCCCCCTCCTGGCCTTCCAGCC  
GCCTCCGACTCTCTCCCCAGGAGTTTGGGGACCATCCCAACATCATCAGCCTCCTTGACG  
TGATCCGGGCAGAGAACGACAGGGACATTTACCTGGTGTGTTGAGTTTATGGACACTGACC  
TGAACGCAGTCATCCGGAAGGGCGGCCTGCTGCAGGACGTCCACGTGCGCTCCATCTTCT  
ACCAGCTCCTGCGGGCCACCCGGTTCCTCCACTCGGGGCACGTTGTGCACCGGGACCAGA  
AGCCGTCCAATGTGCTCCTGGATGCCAACTGCACAGTGAAGCTGTGTGACTTTGGCCTGG  
CCCGCTCCCTGGGCGACCTCCCTGAGGGGCCTGAGGACCAGGCCGTGACAGAGTACGTGG  
CCACACGCTGGTACCGAGCACCGGAGGTGCTGCTCTCTTCGCACCGCTACACCGCTTCCT  
GCCCCAGATACACCCTTGGGGTGGACATGTGGAGTCTGGGCTGTATCCTGGGGGAGATGC  
TGCGGGGGAGACCCCTGTTCCCCGGCACGTCCACCCTCCACCAGCTGGAGCTGATCCTGG  
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CGCCAGACACCTCCCCAGAGGCCTTGGACCTCCTTAGGCGACTCCTGGTGTTCGCCCCGG  
ACAAGCGGTTAAGCGCGACCCAGGCACTGCAGCACCCCTACGTGCAGAGGTTCCACTGCC  
CCAGCGACGAGTGGGCACGAGAGGCAGATGTGCGGCCCCGGGCACACGAAGGGGTCCAGC  
TCTCTGTGCCTGAGTACCGCAGCCGCTCTATCAGATGATCCTGGAGTGTGGAGGCAGCA  
GCGGCACCTCGAGAGAGAAGGGCCCGGAGGGTGTCTCCCCAAGCCAGGCACACCTGCACA  
AACCAGAGCCGACCCTCAGCTGCCTTCTAGGACACCTGTGCAGGGTCCCAGACCCAGGC  
CCCAGAGCAGCCCAGGCCATGACCCTGCCGAGCACGAGTCCCCCGTGCAGCCAAGAACG  
TTCCCAGGCAGAACTCCGCTCCCCCTGCTCCAACTGCTCTCCTAGGGAATGGGGAAAGGC  
CCCCTGGGGCGAAGGAAGCGCCCCCTTGACACTCTCGCTGGTGAAGCCAAGCGGGAGGG  
GAGCTGCGCCCTCCCTGACCTCCCAGGCTGCGGCTCAGGTGGCCAACCAGGCCCTGATCC  
GGGGTGAAGTGAACCGGGGCGGTGGGGTGAGGGTGGCCAGCGTACAACAGGTCCCTCCCC  
GGCTTCCTCCGGAGGCCCCGGCCGGGAGGATGTTTACGACCTCTGCCTTGAGGGTG  
CCCAGGGGGGTGCCAGGGCTTTGCTTGGAGGCTACTCCCAAGCCTACGGGACTGTCTGCC  
ACTCGGCACTGGGCCACCTGCCCTGCTGGAGGGGCACCATGTGTGAGCCGCCCTACTCC  
CTTACCTGGCCCTCTGTTCTTGCCTGCCCCAGCNCCTTCCCCAGACCCCTCTCCAGTCTCCTG  
CACCCCTTAGCCCTCCCTGCTTTGCCTGGCCCGTTGAAGTTCCAGGGAGCTTGCCCGGGT  
CTCCTCGGGGGAGCAGATGAGGGCCCTGCCC

SEQ ID NO: 57\_N28606\_H, MOK\_H

ATGAAGAACTATAAAGCAATTGGCAAAATAGGAGAGGGAACGTTTTCTGAAGTTATGAAG  
ATGCAAAGCCTGAGAGATGGAACTACTATGCATGTAAACAAATGAAGCAGCGCTTTGAA  
AGTATTGAGCAAGTCAACAACCTACGAGAGATCCAAGCACTGAGGCGCCTGAATCCGCAC  
CCAAACATTCTTATGTTGCATGAAGTGGTTTTTGACAGAAAATCTGGTTCTCTTGCACTA  
ATATGTGAACTTATGGACATGAATATTTATGAGCTAATACGAGGGAGAAGATACCCATTA

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FIGURE 2TT

TCAGAAAAAAATTATGCACTATATGTACAGTTATGTAAGTCCCTGGATCATATTCA  
 AGAAATGGAATATTTCCACAGAGATGTAAACCCAGAAAAATATACTAATAAAGCAGGATGT  
 CTGAAATTAGGGGACTTTGGCTCCTGCCGAGTGTCTATTCCCAAGCAGCCGTACACGGAA  
 TACATCTCCACCCGCTGGTACCGGGCCCCGGAGTGTCTCCTCACTGATGGGTTCTACACG  
 TACAAGATGGACCTGTGGAGC3CCGGCTGTGTGTCTTCTACGAGATCGCCAGTCTGCAGCCC  
 CTCTTTCTCTGGAGTAAATGAACTGGACCAAAATCTCAAAAATCCACGATGTCTATCGGACAC  
 CCGGCTCAGAAGATCTCCACCAASTTCAAAAGTCCAGAGCTATGAATTTTGTATTTTCTCT  
 TTTAAAAAGGGATCAGGAATACCTCTACTAACAACCAATTTGTCCCCACAATGCCTCTCC  
 CTCTGACACGCAATGGTGGCTATGATCCCGATGAGAGAATCGCCGCCACCAGGCCCTG  
 CAGCACCCCTACTTTCCAAGAACAGAGGAAAACAGAGAAGCGGGCTCTGGGCAGCCACAGA  
 AAAGCTGGCTTTCCGGAGCACCTGTGGCACCGGAACCACTCAGTAACAGCTGCCAGATT  
 TCCAAGGAGGGCAGAAAGCAGAAACAGTCCCTAAAGCAAGAGGAGGACCGTCCCAAGAGA  
 CGAGGACCGGCTATGTCTATGGAAGTSCCCAACTAAAGCTTTGGGAGTGSTCAGACTG  
 TCGTCTTACTCCAGCCCCACGCTGCAGTCCGTGCTTGGATCTGGAACAAAATGGAAGAGTG  
 CCGGTGCTGAGACCCTTGAAGTGCATCCCTGCGAGCAAGAAGACAGATCCGCAGAAGGAC  
 CTTAAGCCTGCCCCGCAGCAGTGTGCCTGCCACCATAGTGCGGAAAGGCGGAAGATAA

SEQ ID NO: 58\_AB023153\_H, 1CK\_H

ATGAATAGATACACAACAATCAGGCAGCTCGGGGATGGAACCTACGGTTCCGTCTCTGCTG  
 GGAAGAAGCATTGAGTCTGGGGAGCTGATCGCTATTAAAAAAATGAAAAGAAAATTTTAT  
 TCCTGGGAGGAATGCATGAACCAACGGGAGGTTAAGTCTTTAAAGAAGCTCAACCATGCC  
 AATGTAGTCAAATTAAAAGAAGTTATCAGGGAAAATGATCATCTTTATTTTATCTTCGAG  
 TACATGAAGGAAAATCTTTACCAGCTCATTAAGAGAGAGAAATAAGTTGTTTCTGAGTCT  
 GCTATAAGGAATATCATGTATCAGATATTACAAGGACTCGCATTTTATTCACAAACTCGGC  
 TTCTTTTCATCGAGACTTAAAGCCTGAGAACCTCCTCTGCATGGGACCAGAACTTGTGAAA  
 ATTGCAGACTTTGGTTTGGCCCCGAGAAATACGATCAAAACCTCCATATACAGATTATGTA  
 TCTACCAGATGGTACAGGGCTCCAGAAGTACTCCTGAGGTCTACCAACTACAGCTCCCCC  
 ATTGACGTCTGGGCGGTGGGCTGCATCATGGCAGAAGTTTACACCCTCAGGCCACTCTTC  
 CCTGGAGCCAGTGAAATTGACACAATATTCAAAATTTGCCAAGTGCTGGGGACACCAAAA  
 AAGACTGACTGGCCTGAAGGCTATCAACTTTCAAGTGCAATGAACTTCCGTTGGCCACAG  
 TGTGTACCCAATAACTTAAAGACCTTGATTCCCAATGCTAGCAGTGAAGCAGTCCAGCTC  
 CTGAGAGACATGCTTCAGTGGGATCCCAAGAAACGACCAACAGCTAGTCAGGCACCTTCGA  
 TATCCTTACTTCCAAGTTGGACACCCACTAGGCAGCACACACAAAACCTTCAGGATTCA  
 GAAAAACCACAGAAAGGCATCCTGGAAAGGGCAGGCCACCTCCTTATATTAAGCCAGTC  
 CCACCTGCCCCAGCCACCAGCCAAGCCACACACAGCAATTTCTTCACGACAGCATCAAGCC  
 AGCCAGCCCCCTCTGCATCTCACGTACCCCTACAAAGCAGAGGTCTCCAGGACAGATCAC  
 CCAAGCCATCTCCAGGAGGACAAGCCAAGCCCGTTGCTTTTCCCATCCCTCCACAACAAG  
 CATCCACAGTCGAAAATCACAGCTGGCCTGGAGCACAAAATGGTGAGATAAAGCCAAAG  
 AGTAGGAGAAGGTGGGGTCTTATTTCCAGGTCAACAAAGGATTGAGATGATTGGGCTGAC  
 TTGGATGACTTGGATTTTCACTCCATCCCTCAGCAGGATTGACCTGAAAAACAAGAAAAGA  
 CAGAGTGATGACACTCTCTGCAGGTTTGGAGAGTGTTTTGGACCTGAAGCCCTCTGAGCCT  
 GTGGGCACAGGAAACAGTGCCCCCACCAGACGTCTATATCAGCGGCGAGACACGCCACC  
 CTGAGATCTGCAGCCAGCAGCACTATTTGAAGCACTCTCGATACTTGCCTGGGATCAGT  
 ATAAGAAATGGCATACTCTCGAATCCAAGGAATTTATTCACCTAATCATGGTCT  
 AGTTCTGGCTTGTCTGGAATATCTTCAAGGACAATGTGAGTAATCAGCAAGTAATTCAG  
 GTTGGTTCCAGCTCTACAAGTTCTAGTGGAGTACTGGAACTATGTCCCTTCTTCTG  
 AAAAAAGAAATCGGTTCTGCTATGCAGAGGGTACACCTAGCACCTATTCCAGACCTTCC  
 CCTG3TTATTCCTCCCTGAAGGCTATGAGACCTCATCCTGGGCGACCATTCTTGGACACC  
 CAGCCTAGAAGCACTCCTGGGTTGATACCAAGGCTCCAGCCCGCCAGCCAGTGCATGGC  
 CGGACAGACTGGGCTTCCAAGTACCCATCCCGGCGGTGA



FIGURE 2UU

SEQ ID NO: 59\_AAB39940\_M  
AGCAGCAACAATGGTGGCATGAGTGCAGAGGAGGAGATAGGGCCCTGGGCGCTGAGCCCTATG  
AGAGGACCAAGCTTGGCTACAAGGGACTGGAGAGATGAGACTGTTGGGACCAAGAGCCCTG  
CAGCAAGGCATAGACCCAGGAGCAGTGAGCCCTGAGCCCTGGGAAGGACCACGCGAGCCGAG  
GGCCCAGGAAGAACTGAAGCTGGAAGGGTATCTTCTGCTGCAGAGGCTGCCATTGTGGTT  
CTAGATGACAGCGCAGCACCCCCAGCCCTTTTGAACACCGGGTAGTGAGCATCAAAGAT  
ACCCTGATCTCAGCAGGCTACACGGTATCCCAACATGAAGTCTTAGGAGGGGGTTCGGTTT  
GGCCAGGTGCACAGGTGTACAGAGAGGTCTACAGGCCTTGCACTGGCAGCCAAGATCATC  
AAAGTGAAGAACGTAAAGGACCGGGAGGATGTGAAGAATGAGSTCAACATCATGAACCAG  
CTCAGCCACGTAAACTTGATCCAACCTTTATGATGCGTTTGAGAGCAAGAACAGCTTCACT  
CTGATCATGGAGTATGTGGATGGAGGCGAACTCTTTGACCGGATCACGGATGAGAAGTAC  
CACCTCACTGAGTTGGATGTGGTCTTGTTCACGAGGCAGATCTGTGAGGGTGTGCATTAC  
CTGCATCAGCACTATATCCTGCACCTGGACCTCAAGCCTGAGAACATATTGTGTGCAGC  
CAGACAGGGGCATCAAATTAAGATCATTGACTTTGGGCTGGCTAGAAGATACAAGCCCTCGG  
GAGAAGCTAAAGGTGAACCTTTGGTACTCCGGAGTTTCTGGCCCCAGAAGTTGTTAACTAT  
GAGTTTGTGTCAATTTCCAACAGACATGTGGAGTGTGGGAGTTATCACCTACATGCTACTC  
AGTGGTTTGTCCCCATTTCTAGGGGAGACAGATGCAGAGACCATGAATTTTATTGTGAAC  
TGCAGCTGGGATTTTCGATGCTGATACCTTCAAAGGGCTGTGCGAGGAAGCCAAGGACTTT  
GTTTCCCGGTTACTGGTCAAAGAGAAGAGCTGTAGGATGAGCGCCACACAGTGCCTGAAA  
CACGAGTGGTTAAATCACCTGCCTGCCAAAGCCTCGGGCTCCAACGTTTCGCCTCAGATCC  
CAACAACCTGCTGCAGAAATATATGGCTCAGAGTAAATGGAAGAAACATTTCCACGTGGTG  
GCTGCAGTCAACAGGCTACGGAAATTTCCAACGTGTCCCTAATCTTCAACTCTGGTGTTT  
CACTGGGCCTGGGAATTCTTGAGGCAACACGAAGTGGTAATATGAAGAGATTACTCAAGA  
TTTTATGTAGATTGGCGCTTTGCTATTATTGATTTTTTCTTATTTTGCAAAGAATGATGGA  
AGGAAGCAAGAAAGAAAGAAAAGAAGAAAAGGGGGAAGAAAAGGAAAAGGCAGAAAGCAA  
GGAAACAGGCTACGTTGTTGCTCTTCTTGTAGGTGAAAGTGTTTTTTATTAAAAGCCCTAG  
GAATGTTTTTCTGCCTCGTAAGGTACGAGGTCTCATATGCTGCTTGCTACCCCGCACCC  
TTCCTTTTGGTAATAAGAGCAGGCACGCTCAGGATGGGCAGGGAAATCCTACTTGGCTTT  
TGGTCAAATTTGAATTCTAAACTTGTCTATGATTAAAGAAGCCAGTAGGGAGGGAGGTATG  
GAAGAGGGAGGAATTAGGTCCAACAGTGGGGGATGAATTTGACCGAAACATTGTATAAAA  
TTCTTAAAGAATTAATAAAATATATTTTTTAAAGGAG

SEQ ID NO: 60\_AA460132\_H

GGAACCTCAGGCTTCAGAGAGCCGAAAGTTGGGAGGCGTAACCACTTACAGGCCCGAAG  
TGTCCGGGGTGGACGCATTCGGGTAGCCGAAGAAGTCCCAGGATTGCCGAAGAAGTCCCA  
GGATTTCGAAGCGAGCCGAAGCATCGCGACAGTTTTTCAGAGACAGCTGATCGGTTGGAG  
CTGTTGCGCCGAGCAGTCATGGCGGCGGCCAGAGCTACTACGCCGGCCGATGGCGAGGAG  
CCCGCCCCGGAGGCTGAGGCTCTGGCCGCAGCCCGGGAGCGGAGCAGCCGCTTCTTGAGC  
GGCCTGGAGCTGGTGAAGCAGGGTGCCGAGGCGCGCGTGTTCGTTGGCCGCTTCCAGGGC  
CGCGCGGCGGTGATCAAGCACCGCTTCCCCAAGGGCTACCGGCACCCGGCGCTGGAGGCG  
CGGCTTGGCAGACGGCGGACGGTGCAGGAGGCCCGGGCGCTCCTCCGCTGTCGCGCGCT  
GGAATATCTGCCCCAGTTGTCTTTTTTGTGGACTATGCTTCCAAGTGTCTTATATATGGAA  
GAAATTGAAGGCTCAGTGACTGTTTCGAGATTATATTCAGTCCACTATGGAGACTGAAAAA  
ACTCCCCAGGGTCTCTCCAAGTTAGCCAAGACAATTGGGCAGGTTTTGGCTCGAATGCAC  
GATGAAGACCTCATTATGTTGATCTCACCACCTCCAACATGCTCCTGAAACCCCCCTG  
GAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTTTCATTTTCAGCACTTCCAGAG  
GATAAGGGAGTAGACCTCTATGTCTGGAGAAGGCCCTTCTCAGTACCCATCCCAACACT  
GAAACTGTGTTTGAAGCCTTTCTGAAGAGCTACTCCACCTCCTCCAAAAAGGCCAGGCCA  
GTGCTAAAAAAATTAGATGAAGTGCGCCTGAGAGGAAGAAAGAGGTCCATGTTGGGTAG  
AGAATGTGTATGACAACCACACACAGTGAAGCTCTTTTTTCAAAGTAAATTTGAAGAA

## FIGURE 2VV

TGCTACAAGTATGAGATGAGATCTAAGTAAAGGTGTTAAGATATTTTTAAGTGGTATGTG  
ATCGTGTCAATTATCATCTGCACTTCACTCAAGAGCTTACTATGTGTCTAAGTCAATGTTCT  
AGGCAGAATTGGGTATTTAAAGTAAATTGAGGACAGGCTTCTCCAGATTGTGACATGTA  
TATCTCAGATACATGGGTGTGGCATTGAACACATAATGAGAACATTATTCTCTTTTATG  
TCCTTGTGAGACAAGGATGAAGTCTCAGTTGCTGATACTCGCTGAGCTTACTGGCCCTCT  
AACCCAGTGTTTTTTTTTTGTGTTGTTGTGTGTACATGTTATATTTATTTTGAACAGTTT  
AATGGGATACAACCAGCATTTTAAAAAATGAAATAGAATACAGCATGG

SEQ ID NO: 61\_SGK034\_H

CAGAGAGAGAAGGTAAACCAAGGGAACATGCCAGGGCTTCAGAGCACCTTCCTAGCCATG  
GACACGGAGGAGGGGGTAGAGGTGGTGTGGAACGAGCTCCACTTCGGAGACAGGAAGGCC  
TTCGCGGCGCACGAGGAGAAGATCCAGACCGTGTTCGAGCAGCTGGTGCTGGTGGACCAC  
CCGAACATCGTGAAGTTGCACAAGTACTGGCTGGATACCTCTGAGGCCTGCGCGAGGGTC  
ATCTTCATCACAGAGTACGTGTATCAGGCAGCCTCAAGCAATTCCTCAAAAAGACCAAG  
AAGAACCACAAGGCCATGAACGCCCGGGCTGGAAGCGCTGGTGCACGCAGATCCTGTCT  
GCGCTCAGCTTCTGCACGCCTGCAGCCCCCAATCATCCACGGGAACCTGACCAGCGAC  
ACCATCTTCATTTCAGCACACGGCCTCATCAAGATCGGCTCCGTGTGGCACCAGTCTTC  
TCCAATGCACTTCCAGATGATCTCCGAAGCCCCATCCGCGCTGAGCGAGAGGAACTTCGG  
AACCTGCACTTCTTCCCCCAGAGTATGGAGAGGTGGCCGATGGGACCGCTGTGGACATC  
TTCTCCTTTGGGATGTGTGCGCTGGAGATGGCTGTACTGGAAATCCAGACCAATGGGGAC  
ACCCGGGTACAGAGGAGGCCATTGCTCGCGCCAGGCACTCGCTGAGTGACCCCAACATG  
CGGGAGTTCATCCTTTGCTGCCTGGCCCGGGACCTGCCCGCGGGCCCTCTGCCCACAGC  
CTCCTCTTCCACCGCTGCTCTTCGAGGTGCACTCGCTGAAGCTCCTGGCAGCCCCACTGC  
TTCATCCAGCACCACTACCTCATGCCTGAGAATGTGGTGGAGGAGAAGACCAAGGCCATG  
GACCTGCACGCGGTCTTGGCGGAGCTTCCCCGGCCCCGAGGCCCGCTGCAGTGGCGG  
TACTCGGAAGTCTCCTTCATGGAGCTGGACAAATTCCTGGAGGATGTCAGGAATGGAATC  
TACCCACTGATGAACCTTTCAGCCACTCGACCCCTGGGGCTGCCCCGTGTGCTGGCCCCA  
CCCCCGGAGGAGGTCCAAAAGGCCAAGACCCCGACGCCAGAGCCCTTTGACTCTGAGACC  
AGAAAGGTCATCCAGATGCAAGCTGCAACCTGGAGAGAAGCGAGGACAAGGCGCGCTGGCAT  
CTCACTCTGCTTCTGGTGTGGAAGACCGGCTGCACCGGCAGCTGACCTACGACCTGCTC  
CCAACGGACAGCGCCAGGACCTCGCTCGGAGCTCGTGCACTATGGCTTCTCCACGAG  
GACGACCGGATGAAGCTGGCCGCTTCTGGAGAGCACCTTCTCAAGTACCGTGGGACC  
CAGGCCTGACCCGGAGCCCCAGCCCCAGGGGACCATGCCGGGGTGTGCCCCGGGCAGGCC  
ATGTTGGGGAGACTCCAGCACCGTGGGGCTGCCCTCCTCCATGCGCCTGGGAGCACAAAG  
GCCCCGGTAGTGAAGGAACCCCCCTCTCCTGAGAGTGGGGCTGACCCTGCCTTGGGCGC  
CGAGGGGTGGGGGGTGGGTGTGGGGGAGCCGTTAGGCCTCCAGGTCCTTAGGATCAGG  
GTTGCCCCCAGAACCCCTTCCCATATCCTCCATTCTCCGCCCTGAGTTCCTACCCAGGCT  
GCCTGGCTGGGGCCACTGCCTCCTCAGCATGCAGGAGGCTGCCCTGTAGGGAACCCAGC  
TCTGGGGCTTGGGGGTGAGGGTCAGCCCTGGACAGACCTCTGCCAGGGAACCTGCTCCAT  
GGGGTCTGGGAGAGCAGCCATCCCCTGCTGGCACCATAGACCCACACAAGGAGCCTGCAC  
AGCAAGCCAGCGGTGACACACCTGCAGGTGTGAGGCATGGCACTGGGCACAACAGGGACC  
TGGCAGGAGAAACAGACCACAGAGAGGTCTGGAGTTGAGGCTGTTGTGAGCAAGCCCCCT  
GGTCCCACACAGCTCTGCCCTAGAGCCACCTCTTTGACCCCTTACCCACCCTGAGACCAG  
AATTGACGCCCTCTGCAGATCTCCTCTGGCCACTGCAGCCCCTCCAATGGGCTTTTTTC  
TCTCATGCATTCCCTGGCCTGGAGGCTCAGGGACCCACATCCTCCCTGCTCCTCAGAC  
TCACAGCCCCCTCCATGTTACCTCCCGCACCTCCTCCCTGGGGCAGCTGCTCCCTGGGCCT  
CTGAGGATGTCAGCTCCTGGCTCCCTGCCTCTCTCCCACTCCACTCCTGGCTCAGTCTTA  
GAGATTTCTATGCCCTCATGGATTCTACCCCTGCCTTCTGGCCTCTTGATTCTTGGCTT  
GCCTCTCCTCCAATTCCAACTTAGTGAAATGGCCTTAAGCATTTTAACTGTATGTATA  
CATTAGCGCATTCATGCCTTTCTAAACGCATTTCAAATGTCAACCAGGAAGGCACACCAAC

## FIGURE 2WW

TGTATTAGTTTTATACTGCCGCTGTAAAATTTACCACAACTTAGTGACTTAACACAAAT  
TTATTGCAATTCTGTAGGCTGGAAGTCTGACTATGGGTCTCACTGGACTAGAATCAAGGC  
TGGCAGGCTGCCTTCCTTCCTGGAGGTTCTAGGGGAGACTCTGTCTCCTGCTCCTTCAGG  
CTGCTGGCAGAATCCACATCCTTTCCGTGGCAGGGCCAAAGGTCCCCACTTTCTTGCTGA  
TGTAACCTAAGGCCACTTCCAGCTTGTAAGAGGCTGCCTACATTCCTTGCTCCTTGGCCCC  
CTCCTCCATCTTCAGAGCTAGCAGGTTCACTCTGTGTACGAACCATTTCTCTGGTTCCCT  
TGCAGACAGGAAAGGTTGTCCCTAAGGACTCATGAGATTAGGTTGGGCCCAGCCAGATAA  
TACATGATAATCTCCCTCCTCAAGGTTTTTAATATTAAACACATCTGCAGGACACATTTT  
GCCATGTAACTAACATTCCTGCTTCCAGGGATTAAGGAATGAACCTCTTTTGTGGGG  
AAGGGTGGCATTCTGCTGACCACAGCACTCCAACCAAAAGCCAAAACCAAGCAAGACT  
TACTAACGCATATCAAATAAATTAAAGGTACAAAATCGTGAATCTCAGTTATCTTAAATA  
TTCCAATACTATTTACAAAATTATTCAAATTCTCACGCCTTCCAACCTCAAATTAGCAAT  
CTAAAGTAATTTCCATATCCTAGATGGAAACCCTCATGCTAAACTGTCTGATTATGCATG  
GTTCTAAATGGTTTCAGTGGCAAATACATAACATTGTACTACTGATTAAACTGAACTTAA  
AAGC

SEQ ID NO: 62\_AA103218\_M SGK034\_M

CCACGCGTCCGCACCAGAGTATGGCGAAGTCAATGATGGGACTGGCTTTGTGGACATCTT  
CTCCTTCGGGATGTGTGCACTGGAGATGGCTGTACTCGAGATCCAAGCCAACGGGGATAC  
CAGAGTCACAGAAGAGGCCATCGCTCGAGCCAGGCACTCACTGAGTGACCCCAACATGCG  
GGAATTCATCCTCTCCTGCCTGGCCCCGGGACCCTGCCCCGCGACCCTCAGCCCACAACCT  
CCTCTTCCACCGAGTGCTCTTTGAGGTGCACTCGCTGAAGCTGCTGGCAGCTCACTGCTT  
CATCCAGCACCAGTACCTCATGCCTGAGAATGTGGTAGAGGAAAAGACCAAGGCCATGGA  
CCTCCATGCAGTTTTGGCTGAGATGCCGCAGCCCCATGGACCCCCAATGCAGTGGCGGTA  
CTCAGAGGTCTCCTTCTTGGAGCTGGACAAATTCTTAGAGGATGTCAGGAACGGGATCTA  
TCCACTGATGAACTTTGCGGCTGCTCGGCCCTTGGGGCTTCCCCGTGTGTTGGCCCCACC  
CCCAGAGGAAGCCCCAAAAGGCCAAAACCTCCAACGCCAGAACCCTTTGACTCGGAGACCAG  
GAAGGTGGTCCAGATGCAGTGCAACCTGGAAAGAAGCGAGGACAAGGCTCGGTGGCACCT  
TACTCTGCTCTTGGTGCTTGAGGACCGGCTACATCGGCAGCTGACCTATGATCTGCTCCC  
AACGGACAGTGCCCAGGACCTCGCTGCTGAACTAGTGCAATTATGGCTTCCTGCACGAGGA  
TGACAGGACAAAGCTAGCAGCCTTTCTGGAGACCACTTTTCTCAAGTACCGAGGGACGCA  
AGCGTGACCTTCCCAGTCTGACGGCCCAGCAGAGATACAGGGGCTCAGGGTTGTCCACT  
TGGCAAAGAGCCCCCACACTGCTCAAAGCTGCCTTCTGCCTGTGTTCCCTGGAACCTGAAC  
ACAGGCCCTGCTAGTGAAGACACCCCCACCCCCAGCTTTCTGCAGCAGTGTGGGACCCT  
GGGGTGGTGATGGAGCCCTGAGCCTGGACGAGAGTGGATACAGGTCAGTTAGGGGAACCG  
CTCCATCTGGTACTAGACAACAGCCATGCCTTCAGGTGGCATAAGAAACCTAGGGAAGGAG  
CCTGAACTCAGGTGTACAGTGCTGGGCATCAGGCAGACCAGACCTGACCTGATTGGAGA  
ACTGTAGACTAGATAGCTTGGAGTTGAACCCATGGCCAGGGAATTCCTTGGTCTGCTCA  
GACCAGTCTGATCCCTTGACAGACCTGCCTTGAGCCCTCTTTCTGATCTTCCACACTCTT  
GAGACCAGGACCTGTGTCTCTCCCCAAAGCCCTTGGGAAGGATCTTTCTATTTCATCATCCC  
TCTGGCCTAGGGGCTCAGGGGTCAGGCATCCTCCACATTCCCTCCCTGGGGAAGTTGTGT  
GTTTGAGTTGAGGATGTGGGTTCCCTGGCTCCCTCTTTCTCCCCAGCCCAACTTGTCTCTT  
TCTTACTGGTTTCAAAGTCTGATGAACGCTTCCCTCAGAGCCACCCTGGTTTCCTTG  
TTCTTGAACCTGCTCTCTCCCAACTTCAAACCAGGTCTTAAACGTTTTTTAAATGCATAT  
ATAAATGTAATGCAGTCACGGTCTTTTTTAAACACTTTGTGTATGAAACCAGGAAAGCTC  
ACTATTGTATTAGGAATAGTTCCACATTGCTGCTGTTAACAGATATCATAAACCCAGTGG  
TTTGAGACGACACACACACACACACACACACACAGAGAGAGAGAGAGATTCTGTA  
CATCAAGTGTGATCCAGGCTCTCACTAGATTAATACCCAGGCTAAGTTCCCTTTCTGGAAG  
CTGGGACTTACCTCCTGCTCCTTCAAGCTATTGGCAGAACTCACTTCCCTGCAATGGTAA  
GGCAGAAATCCCTATTTTCTCAACAGCTGCCAACTAAGAACCCCTCTCAGCTTCTAGAGG

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## FIGURE 2XX

CCACCAACTTTTCTTAGTTCCTTCTTCTCCCCCTCAAGACCAGCAGCGTCAAGTTGAAT  
CTTTGTCCTGGGCTAGCTGACTGGCTTGCCACTGCTGGGAAGAGTTGGGGCCTTTTGTGA  
GTAGGTGGACCCACCAGGATAACCGAGGATGATCCCCCTTCTCAGGGTCTATAGATGAAC  
CACACCTGCGCAGTTCCTTCTGCTGTCATCCTGGGCTTTGGTGCTTGGAGAACAGCCGTG  
GGCGGTGGGTGTTGTTACTGTGGTACCTACCATGCCATCTTAACCGAAACCAAGACCTAA  
AATAAACAGATTTGTCATGGGACATCTAATAAATTAAATGAACTCTG

SEQ ID NO: 63\_NEK7\_H, N34132\_H

CACGAATCCGAGCCCGCTCGCCTCTCTCCAGCGAACCGACCATGTCTGGCGGCGCCGCAG  
AGAAGCAGAGCAGCACTCCCGGTTCCCTGTTCTCTCGCCGCGGCTCCTGCCCCCAAGA  
ACGGCTCCAGCTCCGATTCTCCGTGGGGGAGAACTGGGAGCCGCGGCGCCGACGCTG  
TGACCGGCAGGACCGAGGAGTACAGGCGCCGCCGACACTATGGACAAGGACAGCCGTG  
GGGCGGCGCGACCACTACCACTGAGCACCGCTTCTTCCGCGGAGCGTCATCTGCG  
ACTCCAATGCCACTGCACTGGAGCTTCCCGGCTTCTCTTCCCTGCCCCAGCCAGCA  
TCCCCGCGGCTGTCCCGCAGAGTGCTCCACCGGAGCCCCACCGGGAAGAGACCGTGACCG  
CCACCGCCACTTCCCAGGTAGCCAGCAGCCTCCAGCCGCTGCCGCCCCCTGGGGAACAGG  
CCGTGCGGGGCCCTGCCCCCTCGACTGTCCCCAGCAGTACCAGCAAAGACCGCCAGTGT  
CCCAGCCTAGCCTTGTGGGGAGCAAAGAGGAGCCGCGCGCGGAGAGTGGCAGCGGCG  
GCGGCAGCGCCAAGGAGCCACAGGAGGAACGGAGCCAGCAGCAGGATGATATCGAAGAGC  
TGGAGACCAAGGCCGTGGGAATGTCTAACGATGGCCGCTTTCTCAAGTTTGACATCGAAA  
TCGGCAGAGGCTCCTTTAAGACGGTCTACAAAGGTCTGGACACTGAAACCACCGTGGAAG  
TCGCCTGGTGTGAACTGCAGGATCGAAAATTAACAAAGTCTGAGAGGCAGAGATTTAAAG  
AAGAAGCTGAAATGTAAAAGGTCTTCAGCATCCCAATATTGTTAGATTTTATGATTCTC  
GGGAATCCACAGTAAAAGGAAAGAGTGCATTGTTTTGGTGACTGAACTTATGACGCTG  
GAACACTTAAACGTATCTGAAAAGGTTTAAAGTGATGAAGATCAAAGTTCTAAGAAGCT  
GGTGCCGTGAGATCCTTAAAGGTCTTCAGTTTCTTCATACTCGAACTCCACTTATCATTC  
ACCGCGATCTTAAATGTGACAACATCTTTATCACCGGCCCTACTGGCTCAGTCAAGATTG  
GAGACCTCGGTCTGGCAACCCTGAAGCGGGCTTCTTTTGCCAAGAGTGTGATAGGTACCC  
CAGAGTTCATGGCCCCCTGAGATGTATGAGGAGAAATATGATGAATCCGTTGACGTTTATG  
CTTTTGGGATGTGCATGCTTGAGATGGCTACATCTGAATATCCTTACTCGGAGTGCCAAA  
ATGCTGCGCAGATCTACCGTTCGCGTGACCAGTGGGGTGAAGCCAGCCAGTTTTGACAAAG  
TAGCAATTCCTGAAGTGAAGGAAATTATTGAAGGATGCATACGACAACAAAGATGAAA  
GATATTCCATCAAAGACCTTTTGAACCATGCCTTCTTCCAAGAGGAAACAGGAGTACGGG  
TAGAATTAGCAGAAGAAGATGATGGAGAAAAATAGCCATAAAATTATGGCTACGTATTG  
AAGATATTAAGAAATTAAAGGGAAAATACAAAGATAATGAAGCTATTGAGTTTTGTTTTG  
ATTTAGAGAGAGATGTCCAGAAGATGTTGCACAAGAAATGGTAGAGTCTGGGTATGTCT  
GTGAAGGTGATCACAAAGACCATGGCTAAAGCTATCAAAGACAGAGTATCATTAATTAAGA  
GGAAACGAGAGCAGCGGCAGTTGGTACGGGAGGAGCAAGAAAACAAAAGCAGGAAGAGA  
GCAGTCTCAAACAGCAGGTAGAACAATCCAGTGCTTCCCAGACAGGAATCAAGCAGCTCC  
CTTCTGCTAGCACCGGCATACCTACTGCTTCTACCACTTCAGCTTCAGTTTCTACACAAG  
TAGAACCTGAAGAACCTGAGGCAGATCAACATCAACAACTACAGTACCAGCAACCCAGTA  
TATCTGTGTTATCTGATGGGACGGTTGACAGTGGTCAGGGATCCTCTGTCTTCACAGAAT  
CTCGAGTGAGCAGCCAACAGACAGTTTCATATGGGTTCCTCAANNATGAACAGGCACATT  
CTACAGGCACAGTCCCAGGGCATATACCTTCTACTGTCCAAGCACAGTCTCAGCCCCATG  
GGGTATATCCACCCTCAAGTGTGCAGCAGGGAATACAGCAGACAGCCCCCTCTCAACAGA  
CAGTGCAGTATTCACCTTTCACAGACATCAACCTCCAGTGAGGCCACTACTGCACAGCCAG  
TGAGTCAGCCTCAAGCTCCACAAGTCTTGCTCAAGTATCAGCTGGAAAACAGAGTACTC  
AGGGAGTCTCTCAGGTTGCTCCTGCAGAGCCAGTTGCAGTAGCACAGCCCCAAGCTACCC  
AGCCGACCACTTTGGCTTCTCTGTAGACAGTGCACATTCAGATGTTGCTTCAGGTATGA  
GTGATGGCAATGAGAACGTCCCATCTTCCAGTGGAAGGCATGAAGGAAGAACTACAAAAC

## FIGURE 2YY

GGCATTACCGAAAATCTGTAAGGAGTCGCTCTCGACATGAAAAAATTCACGCCCCAAAAT  
TAAGAATTTTGAATGTTTCAAATAAAGGAGACCGAGTAGTAGAATGTCAATTAGAGACTC  
ATAATAGGAAAATGGTTACATTCAAATTTGACCTAGATGGTGACAACCCCGAGGAGATAG  
CAACAATTATGGTGAACAATGACTTTATTCTAGCAATAGAGAGAGAGAGTCGTTTGTGGATC  
AAGTGCGAGAAATTATTGAAAAAGCTGATGAAATGCTCAGTGAGGATGTCAGTGTGGAAC  
CAGAGGGTGATCAGGGATTGGAGAGTCTACAAGGAAAGGATGACTATGGCTTTTCAGGTT  
CTCAGAAATTGGAAGGAGAGTTCAAACAACCAATTCCTGCGTCTTCCATGCCACAGCAAA  
TAGGCATTCCCTACCAGTTCTTTAACTCAAGTTGTTCAATTCTGCGGGAAGGCGGTTTATAG  
TGAGTCCTGTGCCAGAAAGCCGATTACGAGAATCAAAGTTTTTCCCCAGTGAAATAACAG  
ATACAGTTGCTGCCTCTACAGCTCAGAGCCCTGGAATGAACTTGTCTCACTCTGCATCAT  
CCCTTAGTCTACAACAGGCCCTTTTCTGAACTTAGACGTGCCCAAATGACAGAAGGACCCA  
ATACAGCACCTCCAACTTTAGTCATACAGGACCAACATTTCCAGTAGTACCTCCTTTCT  
TAAGTAGCATTGCTGGAGTCCCAACCACAGCAGCAGCCACAGCACCAGTCCCTGCAACAA  
GCAGCCCTCCTAATGACATTTCCACATCAGTAATTCAGTCTGAGGTTACAGTGCCCACTG  
AAGAGGGGATTGCTGGAGTTGCCACCAGCACAGGTGTGGTAACTTCAGGTGGTCTCCCCA  
TACCACCTGTGTCTGAATCACCAGTACTTTCCAGCGTAGTTTCAAGTATCACAATACCTG  
CAGTTGTCTCAATATCTACTACATCCCCGTCACTTCAAGTCCCCACATCCACATCTGAGA  
TCGTTGTTTCTAGTACAGCACTGTATCCTTCAGTAACAGTTTCAGCAACTTCAGCCTCTG  
CAGGGGGCAGTACTGCTACCCCAGGTCTTAAGCCTCCAGCTGTAGTATCTCAGCAGGCAG  
CAGGCAGCACTACTGTGGGAGCCACATTAACATCAGTTTCTACCACCACCTTCATTCCCAA  
GCACAGCTTCACAGCTGTCCATTACAGCTTAGCAGCAGTACTTCTACTCCTACTTTAGCTG  
AAACCGTGGTAGTTAGCGCACACTCACTAGATAAGACATCTCATAGCAGTACAACCTGGAT  
TGGCTTTCTCCCTCTCTGCACCATCTTCTCTTCTCCTGAGCAGGAGTGTCTAGTT  
ATATTTCTCAGCCTGGTGGGCTGCATCCTTTGGTCATTCCATCAGTGATAGCTTCTACTC  
CTATTCTTCCCCAAGCAGCAGGACCTACTTCTACACCTTTATTACCCCAAGTACCTAGTA  
TCCCACCCTTGGTACAGCCTGTTGCCAATGTGCCTGCTGTACAGCAGACACTAATTCATA  
GTCAGCCTCAACCAGCTTTGCTTCCCAACCAGCCCCATACTCATTGTCTCTGAAGTAGATT  
CTGATACACAACCCAAAGCTCCTGGAATTGATGACATAAAGACTCTAGAAGAAAAGCTGC  
GGTCTCTGTTTCAGTGAACACAGCTCATCTGGAGCTCAGCATGCCTCTGTCTCACTGGAGA  
CCTCACTAGTCATAGAGAGCACTGTCACACCAGGCATCCCAACTACTGCTGTTGCACCAA  
GCAAACCTCCTGACTTCTACCACAAGTACTTGCTTACCACCAACCAATTTACCCTAGGAA  
CAGTTGCTTTGCCAGTTACACCAGTGGTCACACCTGGGCAAGTTTCTACCCCAGTCAGCA  
CTACTACATCAGGAGTGAAACCTGGAAGTCTCCCTCCAAGCCACCTCTAACTAAGGCTC  
CGGTGCTGCCAGTGGGTACTGAACTTCCAGCAGGTACTCTACCCAGCGAGCAGCTGCCAC  
CTTTTCCAGGACCTTCTCTAACCAGTCCCAGCAACCTCTAGAGGATCTTGATGCTCAAT  
TGAGAAGAACAACCTTAGTCCAGAGATGATCACAGTGACTTCTGCGGTTGGTCTGTGTCCA  
TGGCGGCTCCAACAGCAATCACAGAAGCAGGAACACAGCCTCAGAAGGGTGTCTTCTAAG  
TCAAAGAAGGCCCTGTCTTAGCAACTAGTTTCAGGAGCTGGTGTTTTTAAGATGGGACGAT  
TTCAGGTTTCTGTTGCAGCAGACGGTGCCAGAAAGAGGGTAAAAATAAGTCAGAAGATG  
CAAAGTCTGTTCAATTTTGAATCCAGCACCTCAGAGTCCTCAGTGCTATCAAGTAGTAGTC  
CAGAGAGTACCTTGGTGAAACCAGAGCCGAATGGCATAACCATCCCTGGTATCTCTTCAG  
ATGTGCCAGAGAGTGCCCAAAAATACTGCTCAGAGGCAAAGTCAGACACTGGGCAGC  
CTACCAAGGTTGGACGTTTTTCAGGTGACAACTACAGCAAACAAAGTGGGTCTGTTTCTCTG  
TATCAAAAATACTGAGGACAAGATCACTGACACAAAGAAAGAGGACCAGTGGCATCTCCTC  
CTTTTATGGATTGGAACAAGCTGTTCTTCTGCTGTGATACCAAAGAAAGAGAAGCCTG  
AACTGTCAGAGCCTTACATCTAAATGGGCCGTCTTCTGACCCGGAGGCCGCTTTTTTTAA  
GTAGGGATGTGGATGATGGTTCCGGTAGTCCACACTCGCCCCATCAGCTGAGCTCAAAGA  
GCCTTCTTAGCCAGAATCTAAGTCAAAGCCTTAGTAATTCATTTAACTCCTCTTACATGA  
GTAGCGACAATGAGTCAGATATCGAAGATGAAGACTTAAAGTTAGAGCTGCGACGACTAC  
GAGATAAACATCTCAAAGAGATTTCAGGACCTGCAGAGTCGCCAGAAGCATGAAATTGAAT

## FIGURE 2ZZ

CTTTGTATACCAAACCTGGGCAAGGTGCCCCCTGCTGTTATTATTCCCCCAGCTGCTCCCC  
TTTCAGGGGAGAAGACGACGACCCACTAAAAGCAAAGGCAGCAAATCTAGTCGAAGCAGTT  
CCTTGGGGGAATAAAAGCCCCCAGCTTTCAGGTAACCTGTCTGGTCAGAGTGCAGCTTCAG  
TCTTGCACCCCCCAGCAGACCCCTCCACCCTCCTGGCAACATCCCAGAGTCCGGGCAGAATC  
AGCTGTTACAGCCCCCTTAAGCCATCTCCCTCCAGTGACAACCTCTATTACAGCCTTCACCA  
GTGATGGTGCCATTTTCAGTACCAAGCCTTTCTGCTCCAGGTCAAGGTAATAAAAGCAACCA  
TCATCGTCCAAAAACAATAAAATGGAGATGTTGCCATACCTGGGACAAAAGCCTGTTAAG  
GCGGGTTGGGAGACTAGCTGACCAGAACACAGCCTGTGTGTTGTACACTGAAGAATCTGG  
GTGAAAAGGGGAAGTGGAGTGATAATGAGAATCGGTGGGCTCACTGCTCCCATTAGGTGAA  
ATTACTTTTTTTCAAGGAATTACAGTGAAAAGTTACATCTGTGTGGCCTATATGACTTGC  
TCATTTGGGATTTGGAACCTTAGGCTTTAATATTAGGCTGAGATTTCTTGATGAAATTCT  
AAGGTGTTTTAGCAGTTTCTGAAGCTAATACATTTTCTTAGCCATTGTAGAATTTTGTTA  
CTTTTAAGTATGGGAGTGGCATACTAAAATGAATAACCTTACAATTCAGTTTTTTATCCA  
TAATCTACTTTCCAAATATAGCTCTGTTTATTAGTGATTGCTGAAAAAATTCACACAGAG  
GAAAGAGCTTTTAGTGCATATTAGAACAAGAATTGAAAAGACTTGGGCATCTGGGTGAGAA  
GAATGAAAAAAATATAGGTACTGGCTTATGTGCCTTTGCCACAGTTTCACAGAAATTAGA  
GATCAGTCTCTTCACAGGAAGAATGCACTTGATTGGTAAGGAGGGCAAACCTAGCTAGCAT  
TATTCGAACTAAGAAAAGCTTCCGCATTTTGCAGATGGGTAGAATTAAGACCTAATATTT  
CATCTCTTACATATCTGACCTTCCCCCAGAAGCTTGTTCTTCTGTGTGCCATCTTAGTG  
CATTTACCACTCCAGCCTCAAGTTTCTAACATCTTGATGTTGTGTTCTGTCTCTTCTCC  
TCTCTCTGTTCTACCCTGTTTTTCCCCTCTCACAGGCTGTGCGAAGTTTAACTGTGCATC  
TGAACAGGTGACATTCAAACCTGGTGGCAGGAGGACCCGATTTCTGAGTACGCCCTGCTT  
GGCTCTTTGTGTGTAACACCTTTACTCCTTCTTGTCTTGTGTTTCTGCTGCTTGGATC  
TGATGTTTTCACGCAGTCCATTTTTCATTTGTCTCTTTTTTGTATATCATCTACTCAGTGGCT  
TGGCTGAATTACTGTTACCCTCAGAAGTTTGGGCCCCCACATTAATTATGATAAAAAATG  
TCAAATAACAAGTTATCTACAAATTTCAATGTAACCTTCTGGTAGAAGTGCTTCTTCAT  
GGATCTGTGACAGAGAGTGGATATGGTATCTAGGCAATAGATTGCTGGGTCAATTTAGAAT  
AATGAAGACTGAACTCCACAGTCGTAGTCAGTGCTGTCTGTCTGCCCTAGCATTAGAAAT  
GAGAGAAATCAGCCAGACACGGTGGCCTACACCTGTAATCCCAGCACTTTGGGAGGCCGA  
GGCGGGAAGATTGCTTGAGGCCAGGAGCTCGAGACCAACCCTGGGCAACATGGTGATACC  
CCATCTCT

SEQ ID NO: 64\_BCON3\_H

GCGGAGCGCAGCTGTGAGGGAGTCGCTGTGATCCGGGGCCCCGGAACCCGAGCTGGAGCT  
GAAGCGCAGGCTGCGGGGCGCGGAGTCGGGAGGCCTGAGTGTTCTTCCAGCATGTCGGA  
GGGGGAGTCCCAGACAGTACTTAGCAGTGGCTCAGACCCAAAGGTAGAATCCTCATCTTC  
AGCTCCTGGCCTGACATCAGTGTCACCTCCTGTGACCTCCACAACCTCAGCTGCTTCCCC  
AGAGGAAGAAGAAGAAAGTGAAGATGAGTCTGAGATTTTGGAAGAGTCGCCCTGTGGGCG  
CTGGCAGAAGAGGCGAGAAGAGGTGAATCAACGGAATGTACCAGGTATTGACAGTGCATA  
CCTGGCCATGGATACAGAGGAAGGTGTAGAGGTTGTGTGGAATGAGGTACAGTTCTCTGA  
ACGCAAGAACTACAAGCTGCAGGAGGAAAAGGTTTCGTGCTGTGTTTGATAATCTGATTCA  
ATTGGAGCATCTTAACATTGTTAAGTTTCACAAATATTGGGCTGACATTAAAGAGAACAA  
GGCCAGGGTCATTTTTATCACAGAATACATGTATCTGGGAGTCTGAAGCAATTTCTGAA  
GAAGACCAAAAAGAACCACAAGACGATGAATGAAAAGGCATGGAAGCGTTGGTGCACACA  
AATCCTCTCTGCCCTAAGCTACCTGCACTCCTGTGACCCCCCATCATCCATGGGAACCT  
GACCTGTGACACCATCTTCATCCAGCACAACGGACTCATCAAGATTGGCTCTGTGGCTCC  
TGACACTATCAACAATCATGTGAAGACTTGTCGAGAAGAGCAGAAGAATCTACACTTCTT  
TGCACCAGAGTATGGAGAACTCACTAATGTGACAACAGCAGTGGACATCTACTCCTTTGG  
CATGTGTGCACTGGAGATGGCAGTCTGGAGATTACAGGGCAATGGAGAGTCTCATATGT  
GCCACAGGAAGCCATCAGCAGTGGCATCCAGCTTCTAGAAGACCCATTACAGAGGGAGTT

## FIGURE 2AAA

CATTCAAAAGTGCCTGCAGTCTGAGCCTGCTCGCAGACCAACAGCCAGAGAACTTCTGTT  
CCACCCAGCATTGTTTTGAAGTGCCCTCGCTCAAACCTCCTTGCGGCCCACTGCATTGTGGG  
ACACCAACACATGATCCCAGAGAACGCTCTAGAGGAGATCACCAAAAACATGGATACTAG  
TGCCGTACTGGCTGAAATCCCTGCAGGACCAGGAAGAGAACCAGTTCAGACTTTGTACTC  
TCAGTCACCAGCTCTGGAATTAGATAAAATTCCTTGAAGATGTCAGGAATGGGATCTATCC  
TCTGACAGCCTTTGGGCTGCCTCGGCCCCAGCAGCCACAGCAGGAGGAGGTGACATCACC  
TGTCGTGCCCCCTCTGTCAAGACTCCGACACCTGAACCAGCTGAGGTGGAGACTCGCAA  
GGTGGTGTCTGATGCAGTGCAACATTGAGTCGGTGGAGGAGGGAGTCAAACACCACTGAC  
ACTTCTGCTGAAGTTGGAGGACAACTGAACCGGCACCTGAGCTGTGACCTGATGCCAAA  
TGAGAATATCCCCGAGTTGGCGGCTGAGCTGGTGCAGCTGGGCTTCATTAGTGAGGCTGA  
CCAGAGCCGTTGACTTCTCTGCTAGAAGAGACCTTGAACAAGTTCAATTTTGCCAGGAA  
CAGTACCCTCAACTCAGCCGCTGTACCGTCTCCTCTTAGAGCTCACTCGGGCCAGGCCC  
TGATCTGCGCTGTGGCTGTCCCTGGACGTGCTGCAGCCCTCCTGTCCCTTCCCCCAGTC  
AGTATTACCCTGTGAAGCCCTTCCCTCCTTTATTATTACAGGAGGGCTGGGGGGGCTCCC  
TGGTTCTGAGCATCATCCTTTCCCTCCTCTCTTCTCCTCCTCTGCACTTTGTTTACT  
TGTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCGCCTTCTAGTTGGGGGCTAGT  
CGCTGATCTGCCGGCTCCCCGCCAGCCTGTGTGGAAGGAGGCCACGGGCACTAGGGGA  
GCCGAATTCTACAATCCCGCTGGGGCGGCGGGGCGGGAGAGAAAGGTGGTGTCTGCAGTG  
GTGGCCCTGGGGGGCCATTGATTGCGCTCAGTTGCTGCTGTAATAAAAGTCTACTTTTT  
GCT

SEQ ID NO: 65\_AA711829\_M

CTTAAGCAGTTTCTGAAGAAGACCAAAAAGAACCACAAGACTATGAATGAAAAGGCTTGG  
AAACGCTGGTGTACACAGATCCTCTCTGCCCTAAGCTACCTGCACTCCTGTGACCTCCCC  
ATCATCCATGGGAACCTGACCTGTGACACCATCTTCATCCAGCACAAACGGACTCATCAAG  
ATTGGCTCTGTGGCTCCTGACACTATCAACAATCACGTGAAGACTTGCCGGAAGAACAG  
AAGAACCTACACTTTTTTGCACCAGAGTATGGAGAAGTCACAAACGTGACAACAGCAGTG  
GACATCTACTCCTTTGGCATGTGTGCACTGGAGATGGCAGTGCTGGAGATTCAGGGCAAT  
GGCGAGTCCTCATATGTGCCACAGGAAGCCATCAGCAGTGCCATCCAGCTACTAGAAGAC  
TCATTACAGAGGGAGTTTATTCAAAAGTGCCTGCAGTCTGAGCCTGCTCGGAGACCAACA  
GCCAGAGAACCTTCTGTTCCACCCAGCACTGTTTGAAGTGCCCTCACTCAAGCTTCTTGCT  
GCTCACTGTATCGTGGGGCACCAACACATGATCCCAGAGAACGCTCTAGAGGAGATCACC  
AAGAACATGGATACCAGTGTCTGTACTAGCTGAAATTCCCGCAGGGCCAGGACGAGAACCA  
GTTCACTTTGTACTCTCAGTCACCAGCCCTAGAATTAGACAAATTCCTTGAAGATGTC  
AGGAATGGGATCTACCTCTGACAGCCTTTGGGCTACCTCGGCCTCAGCAGCCACAGCAG  
GAGGAGGTGACATCACCTGTTGTGCCCCCTCTGTCAAGACTCCAACCTCCTGAGCCAGCT  
GAAGTGGAGACACGAAAGGTGGTGTCTGATGCAGTGCAACATCGAATCTGTGGAGGAGGGA  
GTCAAACACCATCTAACACTTCTGCTGAAGCTGGAGGACAAATTGAACCGGCACCTGAGC  
TGTGACCTGATGCCAAATGAGAGCATCCCGGACTTGGCAGCTGAGCTGGTGCAGCTGGGC  
TTCATTAGTGAGGCTGATCAGAGCCGCTGACTTCTCTGCTGGAGGAGACGCTCAACAAG  
TTCAACTTCACCAGGAACAGTACACTCAACACAGCCACTGTCACCGTCTCCTCGTAGAGC  
TCACTTGAGCCAGGCCCTAGCCAGGCTGTGGCTGTCCCTGGGCATGCTGCAGTCTCCT  
GTCCCTTCTCCCCAGTCAGTATTACCCTTCGCGCCCATATTATTTAGGAGGGCTTTAGGG  
GCTCCCTGGTTGAGTATCACCTGCCCCCTTCCCCTCTCTTCCCTCCCCTCTGCACTTTGTT  
TACTTGTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCACCTTCTAGCTGGGGGC  
TAGTAGCTGACCTGCTGCCTCCTGCCCTACTTGTGTGGACAGGAGGCCACGGGCACTGG  
GGAAGCTGAGTTCTACAATCCCGCTGGGGCGCATGGGCAGGAGAGAAAGGTGGTGTCTGCA  
GGGGTGGCCCCCGGGGGGGGCATTGGAATCACCTCAGTTGCTGCTGTAATAAAGTCTAC  
TTTTTGCT

## FIGURE 2BBB

SEQ ID NO: 66\_AA099102\_H

ATGTCATCATGTGTCTCTAGCCAGCCCAGCAGCAACCGGGCCGCCCCCAGGATGAGCTG  
GGGGGCAGGGGCAGCAGCAGCAGCGAAAGCCAGAAGCCCTGTGAGGCCCTGCGGGGGCTC  
TCATCCTTGAGCATCCACCTGGGCATGGAGTCCTTCATTGTGTCAACCGAGTGTGAGCCG  
GGCTGTGCTGTGGACCTCGGCTTGGCGCGGGACCGGCCCTGGAGGCCGATGGCCAAGAG  
GTCCCCCTTGACACCTCCGGGTCCCAGGCCCGGCCCCACCTCTCCGGTCGCAAGCTGTCT  
CTGCAAGAGCGGTCCCAGGGTGGGCTGGCAGCCGGTGGCAGCCTGGACATGAACGGACGC  
TGCATCTGCCCCGTCCCTGCCCTACTCACCCGTCAGCTCCCCGCAGTCCTCGCCTCGGCTG  
CCCCGGCGGCCGACAGTGGAGTCTCACACGTCCTCCATCACGGGTATGCAGGACTGTGTG  
CAGCTGAATCAGTATACCCTGAAGGATGAAATTGGAAAGGGCTCCTATGGTGTGTCGAAG  
TTGGCCTACAATGAAAATGACAATACCTACTATGCAATGAAGGTGCTGTCCAAAAAGAAG  
CTGATCCGGCAGGCCGCTTTTCCACGTCGCCCTCCACCCGAGGCACCCGGCCAGCTCCT  
GGAGGCTGCATCCAGCCCAGGGGCCCATTTAGCAGGTGTACCAGGAAATTGCCATCCTC  
AAGAAGCTGGACCACCCAATGTGGTGAAGCTGGTGGAGGTCTTGATGACCCCAATGAG  
GACCATCTGTACATGGTGTTCGAACTGGTCAACCAAGGGCCCGTGATGGAAGTGCCCAAC  
CTCAAACCACTCTCTGAAGACCAGGCCCGTTTCTACTTCCAGGATCTGATCAAAGGCATC  
GAGTACTTACACTACCAGAAGATCATCCACCGTGACATCAAACCTTCCAACCTCCTGGTC  
GGAGAAGATGGGCACATCAAGATCGCTGACTTTGGTGTGAGCAATGAATTCAAGGGCAGT  
GACGCGCTCCTCTCCAACCTACGTGGGCACGCCCGCCTTCATGGCTCCCGAGTCGCTCTCT  
GAGACCCGCAAGATCTTCTCTGGGAAGGCCAAGGATGTTTGGGCCATGGGTGTGACACTA  
TACTGCTTTGTCTTTGGCCAGTGCCCATTCATGGACGAGCGGATCATGTGTTTACACAGT  
AAGATCAAGAGTCAGGCCCTGGAATTTCCAGACCAGCCCGACATAGCTGAGGACTTGAAG  
GACCTGATCACCCGTATGCTGGACAAGAACCCCGAGTCGAGGATCGTGGTGGCCGAAATC  
AAGCTGCACCCCTGGGTACGAGGCATGGGGCGGAGCCGTTGCCGTCGGAGGATGAGAAC  
TGCACGCTGGTTCGAAGTGACTGAAGAGGAGGTGAGAACTCAGTCAAACACATTCCCAGC  
TTGGCAACCGTGATCCTGGTGAAGACCATGATACGTAAACGCTCCTTTGGGAACCCATTC  
GAGGGCAGCCGGCGGGAGGAACGCTCACTGTACGCGCCTGGAACTTGCTCACCAAAAAA  
CCAACCAGGGAATGTGAGTCCCTGTCTGAGCTCAAGGAAGCAAGGCAGCGAAGACAACCT  
CCAGGGCACCGACCCGCCCGCCCGCTGGGGGAGGAGGAAGTGCTCTTGTGAGAGGCAGTCC  
TGCGTGGAAAGTTGCTGGGGCCCCCGCCCCGGCTCCCCCGCACGCATGCATCCACTGCGG  
CCGGAGGAGGCCATGGAGCCCGAGTAG

SEQ ID NO: 67\_5R69\_17\_2\_H

CCGGGATGTGAGCCTGGTGGTTGGCAGCTGGAGCCACGTCGGAGGGGGAAGTGTGCGAGC  
ATTCTCTGCAGGCATCACAGACCTGAGGCAGTGGCCTCCGGAGGGCACTGGACAGAAACA  
GCCATCCAAGTGGCTGAGTGGAGGGACCCTGCTCAAGTGCAGCTGCAGTGGCCGGGGTTT  
CCCTCAGGTAGGGATCGGGGCGCCTTGTGCGCGCCAGCCACGTGTGGCGTCCGGTACAGT  
CAGCAGAGTGCAGGGTGCGGGCACCAAGAAAGGGGGCGCAGGGGAACTCCCGCGGGCCTC  
GCGTTTGCAAACCTTCTCGCCTGGGCAGGAGGCGGTGCTGGGAAAGAAGGTGGAAGAGCGA  
GCTTTTTTGAACTGTGCACGGGACAGATTGGACGCACACCCCTCGGGAGGCGCGAAGGCA  
TGGAATAATTTGAAGCATATTATCACCCCTTGGCCAGGTCAACACAAACGGTGTGAAGAGA  
TGAAATACTGCAAGAAACAGTGCCCGCGCCTGGGCCACCGCGTCCTCGGCCTGATCAAGC  
CTCTGGAGATGCTCCAGGACCAAGGAAAGAGGAGCGTGCCCTCTGAGAAGTTAACCACAG  
CCATGAACCGCTTCAAGGCTGCCCTGGAGGAGGCTAATGGGGAGATAGAAAAGTTTCAAGCA  
ATAGATCCAATATCTGCAGGTTTCTAACAGCAAGCCAGGACAAAATACTCTTCAAGGACG  
TGAACAGGAAGCTGAGTGATGTCTGGAAGGAGCTCTCGCTGTTACTTCAGGTTGAGCAAC  
GCATGCCTGTTTCACCCATAAGCCAAGGAGCGTCCTGGGCACAGGAAGATCAGCAGGATG  
CAGACGAAGACAGGCGAGCTTTCCAGATGCTAAGAAGAGATAATGAAAAAATAGAAGCTT  
CACTGAGACGATTAGAAATCAACATGAAAGAAATCAAGGAAACTTTGAGGCAGTGTAAGT  
TATCATGTGCCCTGCTGTTTCTGATGGCCCCCAAACCTAGAAGTCATCACTTTACTGGGAC

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## FIGURE 2CCC

CCCAGCCTCCCGCTACCCCTGCATTTGTCCATTTTCTGTGCTGGATGGCTGGAAGCAGCC  
CACAGGTTTGGGGATCCATTCATGGCTAGCCCAGGCTTCTGTCCATGGAATAACATGTGG  
AGAGAGCTTCTTGACCAGTAAGATACCTTCTAGCAGCTGTCAAAGTACTTAAAAACCTCT  
ATGAATAGAATCAAAGCTTCAGTTTCAGTTGCTGAATTTCCAAGAAGAAATTCAAATCAAA  
TTTAAATGCCCACTCATTTCATTTCATTCACAAAACCTGTGAGTATCTGGTTTATGCCAGA  
GGCCATGCAAAGAGGTAACATAAGATGCAGAGAAGGACACTGCCTTCCAGGAGCTCACGGG  
GTGGAGGAGGAAAGAGGAAAGACAGACAGTGAACACACAACAGCAAGGTTACTGAGCTTG  
AACTATGTCCCTAACTACTAGATCTGAAATGACTACGCCAGATGCCAGATGCTCAAGTGC  
CAAGCTCTGGGTAACAGGAATAGACATCCTTCCAGGATGAGAGAGATGAGTCTGGATGAG  
GGTTAAGGCTGGAGGGACAGGCGGGATTTGAAGAGGAGGGAAAGGAAGTGGATGACACAT  
TCTGTTAACTGTCCAGCTGTGTCTCTACTGGTCACTCAGAGGCACGGGAGCCGCTCCCTT  
GGGCTGAGTCCATCAGAAGCCCCAGCCACCACCAGCTCTGGTTCATGTAGTAGAGCTTCC  
CACTCACACATCACAAATATGCCACCTCCCTTAGGACCCCTTCCTCTGCTCATTGACTCT  
TTTGTCTTCTTTCTCTCGGGGGTGAGGTCAGATTTACCACCAAATGCATGCAGGAGAT  
CCCGCAAGAGCAAATCAAGGAGATCAAGAAGGAGCAGCTTTCAGGATCCCCGTGGATTCT  
GCTAAGGGAAAATGAAGTCAGCACACTTTATAAAGGAGAATACCACAGAGCTCCAGTGGC  
CATAAAAGTATTCAAAAAACCTCCAGGCTGGCAGCATTGCAATAGTGAGGCAGACTTTCAA  
TAAGGAGATCAAAACCATGAAGAAATTCGAATCTCCCAACATCCTGCGTATATTTGGGAT  
TTGCATTGATGAAACAGTGACTCCGCCTCAATTCTCCATTGTCATGGAGTACTGTGAACT  
CGGGACCCTGAGGGAGCTGTTGGATAGGGAAAAAGACCTCACACTTGGCAAGCGCATGGT  
CCTAGTCCTGGGGGACAGCCCGAGGCCTATACCGGCTACACCATTGAGAAGCACCTGAACT  
CCACGGAAAAATCAGAAGCTCAAACCTTCCTGGTAACTCAAGGCTACCAAGTGAAGCTTGC  
AGGATTTGAGTTGAGGAAAACACAGACTTCCATGAGTTTGGGAACTACGAGAGAAAAGAC  
AGACAGAGTCAAATCTACAGCATATCTCTCACCTCAGGAACTGGAAGATGTATTTTATCA  
ATATGATGTAAAGTCTGAAATATACAGCTTTGGAATCGTCCTCTGGGAAATCGCCACTGG  
AGATATCCCGTTTCAAGGTGAAGAATGTGAAGACTGGCTCAGCCAGTGGCTGTAATTCCTG  
AGAAGATCCGCAAGCTGGTGGCTGTGAAGCGGCAGCAGGAGCCACTGGGTGAAGACTGCC  
CTTCAGAGCTGCGGGAGATCATTGATGAGTGCCGGGCCCCATGATCCCTCTGTGCGGCCCT  
CTGTGGATGAAATCTTAAAGAACTCTCCACCTTTTCTAAGTAGTGTATCAAAATCTAAA  
CCAAGGAGTCTCTGGACAAGAAGCTGGGAGAGGCACGAACTGGACATCTCTCTCTCAT  
ATCCTTCGGCATTGGGTTATCTATGGGTGCAAGGAGTGGGCACGCTTCTCTGTTACAAAT  
AGAAAACGATTCCAGTCATACAGGACACATCCCACTCCAAATGATATTTCCAAAAACATA  
CCTCTGACAGTAACTTTGATAGATGGTTTGTCAAATGTATCTTTCTGGGTATCCACACCT  
CTTGGCAATGAAATTTGCAGCTCCTCCCTTCATAAATGAAGTCTCTTTCCCCACCATT  
GAATCTGGGCTGGCACTGTGACTTGATTTGATCAATAGAATGTGGAAGAAGTGAAGTGTAT  
GCCAGTTCCAAGCCTAGGTTTCAAGAGGCCTTATAAATGTCTGTTGGAACCTTACCCAGC  
CATGGACATGTTGAGTGAGCATGCTGGAGAATGAGAGACCACATGAAGCAGAAACATGCT  
TTCTAGCTGAAGTCATACTAGCCCAACCAACATGGCAGCTAACACATGAATGAGGCCAA  
TCAAGACCAGAAGAACCACTCAAGCAGATCCCAGCCCAATTGCCCATTCACACAATCAG  
GAGCTAAATAAATTACTGTTGTCTTTT

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CGCCCCGGCCCCCTCCCCCGGCGCCGGCCACGGGAGGCGGTGATGCGGGCGCGGGCGGCCT  
CGGCTGCGCCGAGAGCGGAGACACAGGCTCAAGATGGCAGATTCCGACTGAGGCTGGGGG  
GGCCGAGCTCGCGCGCCGCTTTCCCGTCCCGTTGCCATGAACCGCGGACACCCCGGCC  
CGATGGCCCCCGTGTACGAAGGTATGGCCTCACATGTGCAAGTTTTCTCCCCTCACACCC  
TTCAATCAAGTGCCTTCTGTAGTGTGAAGAACTGAAAATAGAGCCGAGTTCCAACCTGGG  
ACATGACTGGGTACGGCTCCACAGCAAAGTGTATAGCCAGAGCAAGAACATCCCCCTGT  
CGCAGCCAGCCACCACAACCGTCAGCACCTCCTTGCCGGTCCCAACCCAAGCCTACCTT  
ACGAGCAGACCATCGTCTTCCAGGAAGCACCGGGCACATCGTGGTCACCTCAGCAAGCA

## FIGURE 2DDD

GCACTTCTGTCAACGGGCAAGTCTCTGGGCGGACACACAACTAATGGGTGGAAGCACTG  
TGAGCCTCCTTGATACCTACCAAAAATGTGGAATCAAGCGTAAGAGCGAGGAGATCGAGA  
ACACAAGCAGCGTGAGATCATCGAGGAGCATCCACCCATGATTGAGAATAATGCAAGCG  
GGGCCACTGTGGCCACTGCCACCACGTCTACTGCCACCTCCAAAAACAGCGGCTCCAAACA  
GCGAGGGCGACTATCAGCTGGTGAGCATGAGGTACTGTGCTCCATGACCAACACCTACG  
AGGTCTTAGAGTTCTTGGGCGGAGGGACGTTTGGGCAAGTGGTCAAGTGCTGGAACGGG  
GCACCAATGAGATCGTAGCCATCAAGATCCTGAAGAACCACCCATCCTATGCCCGACAAAG  
GTCAGATTGAAGTGAGCATCCTGGCCCGGTTGAGCACGGAGAGTGCCGATGACTATAACT  
TCGTCCGGGCCTACGAATGCTTCCAGCACAAGAACCACACAGTGCTTGGTCTTCGAGATGT  
TGGAGCAGAACCTCTATGACTTTCTGAAGCAAAACAAGTTTAGCCCCCTGCCCTCAAAT  
ACATTGCCCCAGTTCTCCAGCAGGTAGCCACAGCCCTGATGAAACTCAAAGCCTAGGTC  
TTATCCACGCTGACCTCAAACCAGAGAACATCATGCTGGTGGATCCATCTAGACAACCAT  
ACAGAGTCAAGGTCATCGACTTTGGTTTCAGCCAGCCACGTCTCCAAGGCTGTGTGCTCCA  
CCTACTTGCAGTCCAGATATTACAGGGCCCCCTGAGATCATCCTTGGTTTACCATTTTGTG  
AGGCAATTGACATGTGGTCCCTGGGCTGTGTTATTGCAGAATTGTTCCCTGGGTTGGCCGT  
TATATCCAGGAGATTCGGAGTATGATCAGATTCGGTATATTTACAAAACACAGGGTTTGC  
CTGCTGAATATTTATTAAGCGCCGGGACAAAGACAACCTAGGTTTTTCAACCGTGACACGG  
ACTCACCATATCCTTTGTGGAGACTGAAGACACCAGATGACCATGAAGCAGAGACAGGGA  
TTAAGTCAAAGAAGCAAGAAAGTACATTTTCAACTGTTTAGATGATATGGCCCAGGTGA  
ACATGACGACAGATTTGGAAGGGAGCGACATGTTGGTAGAAAAGGCTGACCGGCGGGAGT  
TCATTGACCTGTTGAAGAAGATGCTGACCATTGATGCTGACAAGAGAATCACTCCAATCG  
AAACCCTGAACCATCCCTTTGTCACCATGACACACTTACTCGATTTTCCCCACAGCACAC  
ACGTCAAATCATGTTTCCAGAACATGGAGATCTGCAAGCGTCGGGTGAATATGTATGACA  
CGGTGAACCAGAGCAAACCCCTTTCATCACGCACGTGGCCCCCAGCACGTCCACCAACC  
TGACCATGACCTTTAACAACCAGCTGACCACTGTCCACAACCAGCCCTCAGCGGCATCCA  
TGGCTGCAGTGGCCCAGCGGAGCATGCCCTGCAGACAGGAACAGCCCAGATTTGTGCCC  
GGCCTGACCCGTTCCAGCAAGCTCTCATCGTGTGTCCCCCGGCTTCCAAGGCTTGCAGG  
CCTCTCCCTCTAAGCACGCTGGCTACTCGGTGCGAATGGAAAATGCAGTTCCCATCGTCA  
CTCAAGCCCCAGGAGCTCAGCCTCTTCAGATCCAACCAGGTCTGCTTGCCACGAGGCTT  
GGCCAAGTGGGACCCAGCAGATCCTGCTTCCCCCAGCATGGCAGCAACTGACTGGAGTGG  
CCACCCACACCTCAGTGACGATGCCACCGTGATTCCCGAGACCATGGCAGGCACCCAGC  
AGCTGGCGGACTGGAGAAATACGCATGCTCACGGAAGCCATTATAATCCCATCATGCAGC  
AGCCTGCACTATTGACCGGTCTATGTGACCCTTCCAGCAGCACAGCCCTTAAATGTGGGTG  
TGGCCACGTGATGCGGCAGCAGCCAACCAGCACACCTCCTCCCGGAAGAGTAAGCAGC  
ACAGTCATCTGTGAGAAATGTCTCCACCTGTGAGGTGTCTCCTCTCAGGCCATCAGCT  
CCCCACAGCGATCCAAGCGTGTCAAGGAGAACACACCTCCCCGCTGTGCCATGGTGCACA  
GTAGCCCCGGCCTGCAGCACCTCGGTCACTGTGGGTGGGGCGACGTGGCCTCCAGCACCA  
CCCGGGAAACGGCAGCGGCAGACAATTGTCAATCCCGACACTCCCAGCCCCACGGTCAGCG  
TCATCACCATCAGCAGTGACACGGACGAGGAGGAGGAACAGAAACACGCCCCCACCAGCA  
CTGTCTCCAAGCAAAGAAAAACGTCAATCAGCTGTGTACAGTCCACGACTCCCCCTACT  
CCGACTCCTCCAGCAACACCAGCCCCCTACTCCGTGCAGCAGCGTGCTGGGCACAACAATG  
CCAATGCCTTTGACACCAAGGGGAGCCTGGAGAATCACTGCACGGGGAAACCCCGAACCA  
TCATCGTGCCACCCCTGAAAACCCAGGCCAGCGAAGTATTGGTGGAGTGTGATAGCCTGG  
TGCCAGTCAACACCAGTCACCACTCGTCTCTCTACAAGTCCAAGTCTCCAGCAACGTGA  
CCTCCACAGCGGTCACTCTTCAGGGAGCTCATCTGGAGCCATCACCTACCGGCAGCAGC  
GGCCGGGCCCCCACTTCCAGCAGCAGCAGCCCACTCAATCTCAGCCAGGCTCAGCAGCACA  
TCACCACGGACCGCACTGGGAGCCACCGAAGGCAGCAGGCCTACATCACTCCCAACCATGG  
CCCAGGCTCCGTACTCCTTCCCGCACAAACAGCCCCAGCCACGGCACTGTGCACCCCGCAT  
TGGCTGCAGCCGCTGCGCTGCCACCTCCCCACCCAGCCCCACCTCTACACCTACACTG  
CGCCGGCGGCCCTGGCTCCACCGGCACCGTGGCCCCACCTGGTGGCTCGCAAGGCTCTG

CGCGCCACACCGTGCAGCACACTGCCTACCCAGCCAGCATCGTCCACCAGGTCCCCCGTGA  
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TGAGCCCCGCCAAGGTCAACCAGTACCCTTACATATAAACACTGGAGGGGGAGGGAGGGAG  
GGAGGGAGGGGAGAGAATGGCCCCGAGGGAGGAGGGAGAGAAAGGAGGGAGGCGCTCCTGGGA  
CCGTGGGCGCTGGCCTTTTATACTGAAGATGCCGCACACAACAATGCAAACGGGGCAGG  
GGCGGGGGGGGGGGGGGCAGAGGGCAGGGGGACGGGTGGGGACACCAGTGAAACTTGAACC  
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GGTGGGAAATCTATGGTTTTTTATTTTAAAAAAG

CGGGAGCGAAAGTGCCTGAGCTGAGCTGCACTGTCTGGTGCAGAGATACCGTGGGAGCGCTCGCG  
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TATGACACCTTCATGATGATAGATGAAACCAATGTCCCCCTGTTCAAATGTACTCTGC  
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## FIGURE 2FFF

SEQ ID NO: 70\_AA589241\_M\_DYRK3\_M

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GCAGCAAAGACTGGSCAACCGCACTGAAGGGCTGTGGTGACTACTTGTTCATAGAGTTTC  
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ATCCTTGGATTAGCAAGTCTACACCCAAACCTCTCACCATGGACAAGGTGCCAGGGAAGC  
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SEQ ID NO: 71\_5R72\_16\_2\_H

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## FIGURE 2GGG

CCTGGCCAAGGATGACCGAGCTGCACGCGGGCAGCCGGCGAGCGACACAGACGGCCTGGA  
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## FIGURE 2HHH

TCATCATAATTTAAAATTAAATTCTAAGAAGAGGCTGGGTGCAGTGGCTCACACCTTTAA  
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CCT

SEQ ID NO: 73\_R43524\_H, HRI\_H

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CAGCACTTAACGAGAAGGAACCTCATCGCAGAGACCATCTGCCATTTCAGCTGCTGCAGAGT  
GAACTTTTCCAAAATTCTGGAAATGTTAACCTCACCTACAGATGAAGATAATAGAGCAA  
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SEQ ID NO: 74\_17000057519457\_H

CACAAGAGCCCTTCCTGCAGGGAACCTCAGGCTTCAGAGAGCCGAAAAGTTGGGAGGCGT  
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## FIGURE 2III

AGGTTTTGGCTCGAATGCACGATGAAGACCTCATTCATGGTGATCTCACCACCTCCAACA  
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SEQ ID NO: 75\_AA013524\_M

CTGGTGCAAGAGGGCGCCGAGGCGCGCGTTTTCCGTGGCCGCTTCCAGGGCCGCGCGGCC  
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GCCCCAGTCGTCTTCTTTGTGGAATATGCGTCTAACTGCTTATATATGGAAGAAATCGAA  
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TGCCTCTTGGACCTGGCCAGGAGGATGGGGCAGGTTCTGGCCGGAATGCACGACCAAGAC  
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## FIGURE 2JJJ

GTCGACCTCTATGTCCTGGAGAAGGCCTTCCTCAGCACGCACCCCCACACCGAGACCGCG  
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GGTTGTTAAGTGGTCTGTGATCGTGCTGGGCCACCACCATCCATGGCTCACTGTTCTCAG  
GGGCTTCATGTACATGAGGTTTATTCTGGGCAGAACTGGGTAGGTAGCCAGGCTAGCCT  
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SEQ ID NO: 76\_17000139801197\_H, IRAKM\_H

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AAGTCCTTCAGGTGTCTTCTCCTCTATTCCTGGAGAATGTACCAAGTATTCAGTGGA  
GATGATGAAAGCCAGAATAACAATTTACTACCTTCTGATGAAGGCCTGAGGATAGACAGA  
ATGACTCAGAAAACCTCTTTTGAATGCAGCCAGTCTGAGGTTATGTTTCTGAGCTTGGAC  
AAAAAGCCAGAGAGCAAGAGAAATGAGGAAGCTTGCAACATGCCAGTTCTTCTTGTGAA  
GAAAGTTGGTTCCCAAAGTATATAGTTCCATCCCAGGACTTAAGGCCCTATAAGGTAAAT  
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ATGTGGAAGAGATTTTATCAGAACTGGAAGTTCTACTCCTGTTCCGTCACCCCCACATA  
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AGCAACGGGACGCTTTTCGACAGATTACAGTGCACAAATGGCACAAACCCGCTTTCCTGG  
CACGTTGCAATCAGCGTATTGATAGGAATAGCCAAAGCCATCCAACTTGCACAACACT  
CAGCCGTGCGCCGTCATCTGTGGCAACGTTTCCAGTGCAAAACATACTCTTGGATGACCA  
CTCCAAACCCAACTAACGGATTTTGCTGCAGCGCACCTTCGACCCCAATCTAGAGCAGCAG  
AGTTCTACCATAAATATGACCGGGCGGTGGCAGGAAACATCTGTGGTACATGCCAGAAGAA



## FIGURE 2KKK

TACATCAGACAGGGAAGACTTTCCGTTAAAACTGATGTCTACAGCTTCGGAATCGTGATC  
ATGGAGGTTCTAACGGGCTGCAAAGTGGTGCTGGATGACCCGAAACACGTTTCAGCTGCGG  
GACCTCCTCATGGAAGTCTGAGAGAAAAGAGGCCTAGACTCCTGCCTGTCCTTCTTAGAC  
AGGAAGATACCACTGTCTCGGAACTTCTCTGCAAAGCTCTTCTCTCTGGCGGGCCGG  
TGTGTGGCAACGAAGGCCAAGTTAAGACCCACGATGGACGAAGTCCTGTCCTCTCTGGAG  
AGCACCACAGCCTAGCTTGTATTTTGCAGAAGACCCCTCCCACGTCCTTGAAGTCCTTCAGG  
TGTCTTCTCCACTGTTCTTGGATAATGTCCCAAGTATTCCAGTAGAAGATGATGAAAAC  
CAGAATAACCATTTCAGTACCTCCCAAGGAAGTTTGGGGACAGATAGAGTGACTCAGAAA  
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CCAGAGCTTGTGGCGCCATCCCAGGACTTAAGTCCTACTGTGATCAGTTTGGGCTCGTCT  
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AAAAATAAAGCAAACGTCACTGAAGGCACTGAGCAAATAGCATCCCCGTGAAAAGACACG  
AGCTCTGAGCTCCGTGAGTACAGCCAAGGGACCAACTGATGGAGAATTTGAATGGTGCAG  
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AAGATTCCGGGTCTGACAACCAAAACCTAGCAAAGAGTAGCAGGACAAGTCTCTCTCTT  
AAGTCTCTCACTCTCTCTCATCATCCGAGTGAGATCTTGGTATAGGTGAACAGAGAACCA  
CCCACCTTCCAGAACCAGAACCACCTTCTCCCCAAGCCAGCAGTCAGTCACTCACCATCA  
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CTACGTCCTTTATAAAACCCAGGTCTTCAGGGCCCCACCCCTTTCTTTTCCATCCTTGCT  
CAGAGGCAGCCTTTTGTATACATTCCCTGACCCCCACCCCAATTATATCTCTCATATGATA  
TCTGTTGCGTAGTGTGACTTTGTGGCATGACTTGGTTGTGAGATCATTTCACACAAGAACA  
AGCGAATACACAACAACAAAGCCCACCATCATTACCACCGGCACTTAATGCTAGTCTTTC  
TGCTAGGGATACTGACAGTCTATTTGCTTCCCATGGTCATAGGGAAGTTGCTCAAATGCA  
AAGGTTGTAGGGAATGTCTAATTTGTAAATGGCGTCGGGTGCCTTTGGAAGGAATTGTGT  
TTTTACAGCCAGTTGCTACTCTTGTTTATCGCTGGTTAACCGGTCTGTCCGGAAGTGAGC  
CAAGTCATCCTTGCTAGGGCTTTTTCTGTGTAGAGAGGGAATTCCAGTCCAAAGTCTGCT  
TCTCTGTATTTAAATTCTTAGAAGAGTTGCCTGTGGCATTCCAATTGTTATATAAAAAAA  
TTATATTAAAGAATTCCAGCACT

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ATGGCGAGTGCGGTGAGGGGTGAGGCCGTGGCCCCGGCTGGGGCTCCAGCTCCAGTTCC  
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CTGCTGGTGTCCACCTTGGATGGAAGTCTCCACGCACTAAGCAAGCAGACAGGGGACCTG  
AAGTGGACTCTGAGGGATGATCCCGTCATCGAAGGACCAATGTACGTACAGAAATGGCC  
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GATGGGGTCTTCTACACAGGCCGGAAGCAGGATGCCTGGTTTGTGGTGGACCCTGAGTCA  
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CGAACACAGTATACGGTCACCATGCATGACCCAAGAGCCCCAGCCCTGCGCTGGAACACC  
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CGCCAGCTGCCGCATCTCACGCTGGCTCGAGACACTCTGCATTTCTCGCCCTCCGCTGG  
GGCCACATCCGACTGCCTGCCTCAGGCCCCCGGGACACAGCCACCCCTCTTCTCTACCTTG  
GACACCAGCTGCTAATGACGCTGTATGTGGGGAAGGATGAAACTGGCTTCTATGTCTCT  
AAAGCACTGGTCCACACAGGAGTGGCCCTGGTGCCTCGTGGACTGACCCTGGCCCCCGCA  
GATGGCCCCACCAAGATGAGGTGACACTCCAAGTCTCAGGAGAGCGAGAGGGCTCACCC

## FIGURE 2LLL

AGCACTGCTGTTAGATACCCCTCAGGCAGTGTGGCCCTCCCAAGCCAGTGGCTGCTCAT  
GGACACCACGAGCTACCCCCAGTCCTGCACACCACCATGCTGAGGGTCCATCCCACCCCTG  
GGGAGTGGAACTGCAGAGACAAGACCTCCAGAGAATAACCCAGGCCCCAGCCTTCTTCTTG  
GAGCTATTGAGCCTGAGCCGAGAGAACTTTGGGACTCCGAGCTGCATCCAGAAGAAAAA  
ACTCCAGACTCTTACTTGGGGCTGGGACCCCAAGACCTGCTGGCAGCTAGCCTCACTGCT  
GTCTCTCTGGGAGGGTGGATTCTCTTTGTGATGAGGCAGGTGGTGGAGAAGCAGCAGGAG  
ACCCCCCTGGCACCTGCAGACTTTGCTCACATCTCCCAGGATGCCAGTCCCTGCACCTCG  
GGGGCCAGCCGGAGGAGCCAGAAGAGGCTTCAGAGTCCCTCAAAGCAAGCCCAGCCACTC  
GACGACCCTGAAGCTGAGCAACTCACCGTAGTGGGGAAGATTTCTTCAATCCCAAGGAC  
GTGCTGGGCCCGGGGCGAGGCGGGACTTTCGTTTTCCGGGGACAGTTTGAGGGACGGGCA  
GTGGCTGTCAAGCGGCTCCTCCGCGAGTGCTTTGGCCTGGTTCGGCGGGAAGTTCAACTG  
CTGCAGGAGTCTGACAGGCACCCCAACGTGCTCCGCTACTTCTGCACCGAGCGGGGACCC  
CAGTTCCACTACATTGCCCTGGAGCTCTGCCGGGCCTCCTTGCAAGGAGTACGTAGAAAAC  
CCGGACCTGGATCGCGGGGGTCTGGAGCCCGAGGTGCTGCTGCAGCAGCTGATGTCTGGC  
CTGGCCCCACCTGCACTCTTTACACATAGTGCACCGGGACCTGAAGCCAGGAAATATTCTC  
ATCACCGGGCCTGACAGCCAGGGCCTGGGCAGAGTGGTGCTCTCAGACTTCGGCCTCTGC  
AAGAAGCTGCCTGCTGGCCGCTGTAGCTTCAGCCTCCACTCCGGCATCCCCGGCACGGAA  
GGCTGGATGGCGCCCCGAGCTTCTGCAGCTCCTGCCACCAGACAGTCTTACCAGCGCTGTG  
GACATCTTCTCTGCAGGCTGCGTGTCTACTACGTGCTTTCTGGTGGCAGCCACCCCTTT  
GGAGACAGTCTTTATCGCCAGGCAAACATCCTCACAGGGGCTCCCTGTCTGGCTCACCTG  
GAGGAAGAGGTCCACGACAAGGTGGTTGCCCGGGACCTGGTTGGAGCCATGTTGAGCCCA  
CTGCCGCAGCCACGCCCCCTTGCCCCCAGGTGCTGGCCCCACCCCTTCTTTTGGAGCAGA  
GCCAAGCAACTCCAGTTCTTCCAGGACGTCACTGACTGGCTGGAGAAGGAGTCCGAGCAG  
GAGCCCCCTGGTGAGGGCACTGGAGGCGGGAGGCTGCGCAGTGGTCCGGGACAACCTGGCAC  
GAGCACATCTCCATGCCGCTGCAGACAGATCTGAGAAAGTTCCGGTCTCTATAAGGGGACA  
TCAGTGCGAGACCTGCTCCGTGCTGTGAGGAACAAGAAGCACTACAGGGAGCTCCCA  
GTTGAGGTGCGACAGGCACTCGGCCAAGTCCCTGATGGCTTCGTCCAGTACTTCACAAAC  
CGCTTCCCACGGCTGCTCCTCCACACGCACCGAGCCATGAGGAGCTGCGCCTCTGAGAGC  
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GGGAGGTGA

SEQ ID NO: 79\_HGP\_6644466

GGAGGGTTCGAATTGCAACGGCAGCTGCCGGGCGTATGTGTTGGTGCTAGAGGCAGCTGC  
AGGGTCTCGCTGGGGCCGCTCGGGACCAATTTTGAAGAGGTACTTGGCCACGACTTATT  
TTCACCTCCGACCTTTCTTCCAGGCGGTGAGACTCTGGACTGAGAGTGGCTTTCACAAT  
GGAAGGGATCAGTAATTTCAAGACACCAAGCAAATTATCAGAAAAAAGAAATCTGTATT  
ATGTTCAACTCCAATAATAATATCCCGGCCTCTCCGTTTATGCAGAAGCTTGGCTTTGG  
TACTGGGGTAAATGTGTACCTAATGAAAAGATCTCCAAGAGGTTTGTCTCATTTCTCCTTG  
GGCTGTAAAAAAGATTAATCCTATATGTAATGATCATTATCGAAGTGTGTATCAAAGAG  
ACTAATGGATGAAGCTAAGATTTTGAAGAGCCTTCATCATCCAAACATTTGTTGGTTATCG  
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CATAATTTTAAAAGTTGCTTTGAATATGGCAAGAGGGTTAAAGTATCTGCACCAAGAAAA  
GAAACTGCTTCATGGAGACATAAAGTCTTCAAATGTTGTAATTAAAGGCGATTTTGAAGC  
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TGGTGTATTACTGACAAGGCAGACATATTTGCCTTTGGCCTTACTTTGTGGGAAATGAT  
GACTTTATCGATTCCACACATTAATCTTTCAAATGATGATGATGATGAAGATAAACTTT  
TGATGAAAGTGATTTTGATGATGAAGCATACTATGCAGCGTTGGGAACCTAGGCCACCTAT  
TAATATGGAAGAACTGGATGAATCATACCAGAAAGTAATTGAACTCTTCTCTGTATGCAC

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## FIGURE 2MMM

TAATGAAGACCCTAAAGATCGTCCTTCTGCTGCACACATTGTTGAAGCTCTGGAAACAGA  
TGTCTAGTGATCATCTCAGCTGAAGTGTGGCTTGGCTAAATAACTGTTTATTCCAAAATA  
TTTACATAGTTACTATCAGT'AGTTATTAGACTCTAAAATTGGCATATTTGAGGACCATAG  
TTTCTTGTTAACATATGGATAACTATTTCTAATATGAAATATGCTTATATTGGCTATAAG  
CACTTGGAATTGTACTGGGTTTTCTGTAAAGTTTTAGAACTAGCTACATAAGTACTTTG  
ATACTGCTCATGCTGACTTAAAACACTAGCAGTAAAACGCTGTAACTGTAAACATTAAAT  
TGAATGACCATTACTTTTTATTAATGATCTTTCTTAAATATTCTATATTTTAATGGATCTA  
CTGACATTAGCACTTTGTACAGTACAAAATAAAGTCTACATTTGTTTAAAACACTGAACC  
TTTTGCTGATGTGTTTATCAAATGATAACTGGAAGCTGAGGAGAATATGCCTCAAAAAGA  
GTAGCTCCTTGGATACTTCAGACTCTGGTTACAGATTGTCTTGATCTCTTGGATCTCCTC  
AGATCTTTGGTTTTTGTCTTAATTTATTAAATGTATTTTCCATACTGAGTTTAAAATTTA  
TTAATTTGTACCTTAAGCATTTCAGCTGTGTAAAAACAATAAACTCAAATAGGATGA  
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ATCTCCAAGAGGGTTGTCTCATTCTCCTTGGGCCGTGAAAAAGATAAGTCTTTTATGCGA  
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CCTTAATCACCCAAACATTATAGGATATCGTGTCTTTACTGAAGCCAGTGATGGTAGTCT  
GTGCCTTGCTATGGAGTATGGAGGTGAAAAGTCTCTGAATGACTTAATAGAAGAGCGGAA  
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CAGAGGGCTAAAGTACCTGCACCAAGAAAAGAAGCTGCTTCATGGAGACATAAAGTCTTC  
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AGATGATGATGTTGATGAAGATGCAACCTTTGATGAGAGTGACTTCGATGATGAAGCATA  
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GAAGGCCATTGAACTCTTCTGTGTGTGCACTAATGAGGATCCTAAAGATCGCCCGTCTGC  
TGCACACATCGTTGAAGCTTTGGAAGTAGATGGCCAATGTTGTGGTCTAAGCTCAAAGCA  
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CCATTGCTTTGTTACAGATCTTTTTAGATATTCTTGCTTCTTTAGTGGGTACTAAAAAT  
TTCACTACGTACATGTGGTACAGATATCTGTCTGCTCATAGTGTGAGTCCTTCAGCTGGC  
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SEQ ID NO: 81\_5R57\_10\_2\_M TESK2\_M

GCTGCTGGACAGTGACTTGTATTTACCGTGGACTGTGAGAGTGAACTGGCCTATGGCAT  
AGCAGTGGGCCCTCAGCTACCTTCACTTCAAAGGCATTTTCCATCGGGACCTCACATCAA  
GGTGTGAAGGCTTTGCTTTC

SEQ ID NO: 82\_AA232253\_H

ATGTCGTCTCTCGGTGCCTCCTTTGTGCAAATTAAATTTGATGACTTGCAGTTTTTTGAA  
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AGTCACAGAAACATCATCCAGTTTTATGGAGTAATTCTTGAACCTCCCAACTATGGCATT  
GTCACAGAATATGCTTCTCTGGGATCACTCTATGATTACATTAACAGTAACAGAAGTGAG  
GAGATGGATATGGATCACATTATGACCTGGGCCACTGATGTAGCCAAAGGAATGCATTAT  
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## FIGURE 2NNN

ATAGCTGCTGATGGAGTATTGAAGATCTGTGACTTTGGTGCCTCTCGGTTCATATAACCAT  
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CAGTGTGGGAAGCTGATGCCAAGAAACGGCCATCATTCAAGCAAATCATTTCAATCCTG  
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GCGGAGTGGAGGTGCGAAATTGAGGCAACTCTTGAGAGGCTAAAGAAACTAGAGCGTGAT  
CTCAGCTTTAAGGAGCAGGAGCTTAAAGAACGAGAAAGACGTTTAAAGATGTGGGAGCAA  
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GCACTCAATCCTCACCAGTCGCCTGACTTCAAGAGAAGCCCCAGGGACCTCCACCAACCC  
AACACCATAACCAGGGATGCCTTTGCACCCTGAGACTGACTCAAGAGCCAGTGAAGAGGAC  
AGCAAAGTCAGCGAAGGGGGCTGGACAAAAGTGGAAATACCGGAAAAAGCCCCACAGGCCA  
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TGA

SEQ ID NO: 83\_AI375137\_H

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GAAGAAGGCAGCAAAGCAGATGTGAATGCTCAAGATAATGAAGACCATGTCCCACTCCAT  
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## FIGURE 2000

GGCAAATTTGAAGTTGCCAAGGAAATCATCCAAATATCAGGAACAGAAAGTCTGACTAAG  
GAAAACATCTTCAGTGAAACAGCTTTTCATAGTGCTTGACCTATGGCAAGAGCATTGAC  
CTAGTCAAATTTCTTCTTGATCAGAATGTCATAAACATCAACCACCAAGGAAGGGATGGG  
CACACTGGATTACACTCTGCTTGCTACCACGGTCACATTCGCCTGGTTCAGTTCTTACTG  
GATAATGGAGCTGATATGAATCTAGTGGCTTGATGCCAGCAGGTCTAGTGGTGAAAAA  
GATGAGCAGACATGTTTGATGTGGGCTTATGAAAAAGGGCATGATGCCATTGTCACTC  
CTGAAGCATTATAAGAGACCACAAGATGAATTGCCCTGTAATGAATATTCTCAGCCTGGA  
GGAGATGGCTCCTATGTGTCTGTTCCATCACCTTGGGGAAGATTAAGAGCATGACAAAA  
GAGAAGGCAGATATTCTCCTCCTAAGAGCTGGATTGCCTTCACATTTCCATCTTCAGCTC  
TCAGAAATTGAGTTCATGAGATTATTGGCTCAGGTTCTTTTGGGAAAGTATATAAGGA  
CGATGCAGAAATAAAATAGTGGCTATAAAACGTTATCGAGCCAATACCTACTGCTCCAAG  
TCAGATGTGGATATGTTTTGCCGAGAGGTGTCCATTCTCTGCCAGCTCAATCATCCCTGC  
GTAATTCAGTTTGTGGGTGCTTGCTTGAATGATCCCAGCCAGTTTGCCATTGTCACTCAA  
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CAGTCTAAATTAATTATTGCAGTAGATGTTGCCAAAGGCATGGAGTACCTTCACAACCTG  
ACACAGCCAATTATACATCGTGACTTGAACAGTCACAATATTCTTCTCTATGAGGATGGG  
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ATGACAAAACAACCTGGGAACCTCCGTTGGATGGCTCCTGAGGTGTTACGCAGTGCCT  
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GGCGAAATTCCATTGCTCATCTCAAGCCAGCGGCTGCGGCAGCAGACATGGCTTACCAC  
CACATCAGACCTCCCATTTGGCTATTCCATTCCCAAGCCCATATCATCTCTGCTGATACGA  
GGGTGGAACGCATGTCCTGAAGGAAGACCCGAATTTTCTGAAGTTGTATGAAGTTAGAA  
GAGTGTCTCTGCAACATTGAGCTGATGTCTCCTGCATCAAGTAACAGCAGTGGGTCTCTC  
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ATGATTTCTTGCTGTNATAACCTATGCACTCACAAAGATGAACTCTCTGAGAGGGATGA  
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GCTTTATCGCCAGCTAATTGACCTGGGCTATCTGAGCAGCAGTCACTGGAAGTGTGGGGC  
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CTTGAGCACATTTTCTCACCAGGTGTTACAGACTCGCCTGGTGGATGCAGCCAAGGCCCT  
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GGACCTGCAGATCACTCCCAAACGTCTGGAATATACTCGAAAAAAGGAGAATGAGTTGTA  
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## FIGURE 2PPP

TTTACAGGATGTCTTGCTTCATCGTAAACCTAAACTGGGACAGGAACTGGGCCGGGGCCA  
GTATGGTGTGGTATACCTGTGTGACAACTGGGGAGGACACTTCCCTTGTGCCCTCAAATC  
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GGAGGGAATCCGCTTCCCTGCACAGCCAGGGACTTGTCCATCGTGATATCAAACCTGAAAAA  
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AGGGAAGTACGATAATTCCGTGGATGTCTACGCTTTTGGAAATTCCTTTTCTGGTATATCTG  
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GAACAATGTGCGGAGGGGGGCTCGCCCAGAACGTCTTCCTGTGTTTGATGAGGAGTGCTG  
GCAGTTGATGGAAGCCTGTTGGGATGGCGACCCCTTGAAGAGGCCTCTCTTGGGCATTGT  
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TCCTTCCCCCTCACCATTTGGCCATGGGGAGAATTTGACATTTATTCATATAGGACACA  
CTCCCAAGGGAACCTGGTGTCTGCTGGGAACTTGGAACTTCCCAGGCAGGGATGACTCC  
TGGACAGTGAAGAGTTGAATGACTGAGCATATTCAGCAGCTCACTGAAGCGCCAAGCTAT  
CCCTTTAGCAAAAAAGTGTCTCAGATGTGTAAAAGCTGAGGAATGTGGTGTCTGGCTTC  
ACAAATGAAAAGGAGGCAGATGTT

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TTGATGTCAACCTGAAGGCTTCTAAAGCGAGTGATGTCTACAGCTTTGGGATCCTCGTGT  
GGCAGTGCTGGCTGGCAGAGAAGCTGAGTTGGTAGACAAGACTTCACTAATCCGGGAAA  
CAGTGTGTGACAGGCAGAGTCGTCCCTCCACTGACAGAGCTGCCTCCAGGTAGCCCTGAGA  
CTCCCGGCTTGGA AAAACTGAAGGAGTTAATGATTCAATTGCTGGGGTTCCAGTCCGAAA  
ACAGGCCATCCTTCCAGGACTGCGAACC AAAACCAATGAAGTTTACAATCTGGTAAAGG  
ACAAGGTAGATGCTGCTGTCTCCGAGGTAAAGCATTATCTGTCTCAGCACAGAAGCAGCG  
GCAGAACTTGTCTGCCAGAGAGCCAAAGCCAAAGAGGCACAGAAATGGATTGCCCGAGGG  
AAACCATGGTTTCTAAAATGCTGGACCGCCTGCATTTGGAGGAACCTCCGGACCAGTTC  
CTGGAAAATGTCTTGAGAGGCAAGCACAGGACACATCAGTTGGGCCTGCCACACCAGCAA  
GGACATCTTCTGACCCCGTGGCTGGCACTCCTCAGATTCCACATACTTTACCCTTCAGAG  
GCACAACACCTGGGGCCAGTCTTTACTGAGACTCCCGGTCCTCACCCCCAAAGGAATCAGG  
GAGATGGAAGACACGGCACTCCTTGGTATCCCTGGACCCCAACGAATCCAATGACAGGGC  
CACCGGCTCTCGTCTTCAACAACCTGTTCTGAAGTGCAGATTGGGAACTACAACCTCCTTGG  
TAGCACCACCAAGAACTACTGCCTCAAGTTCGGCCAAGTATGACCAAGCACAGTTCGGCA  
GGGGTAGGGGCTGGCAGCCCTTCCACAAGTAGACTTCAGAGAATCACTGCAAGAGCCTGA  
AGTGTGCCATTGAGCGTGGCAATAAAAAGCACGTTTTAAGCAACCTGGACTGGCTAAGAC  
AGTCCTTGCCACTTCCTGAAGCTCACAACTTCTGTGAGGACAGTTGGACCTACACCCAA  
ACTGACTCTTGACCCATCTCCTTAAAGTCAATAAACATAGCATGTAACTGTG

SEQ ID NO: 86\_AA744236\_H

ATGGGATCAGAGAACAGTGCTTTAAAGAGCTATACACTGAGAGAACCACCATTTACCTTA  
CCCTCTGGACTTGCTGTTTATCCCGCTGTACTGCAAGATGGCAAATTTGCTTCAGTTTTT  
GTGTATAAGAGAGAAAAATGAAGACAAGGTTAATAAAGCTGCCAAGCATTTGAAGACACTT  
CGTCACCCCTTGCTTGCTAAGATTTTTATCTTGTAAGTGTGGAAGCGGATGGCATTCATCTT  
GTCAGTGAGCGAGTACAGCCCCCTGGAAGTGGCTTTGGAAACATTGTCTTCTGCAGAGGTC  
TGTGCTGGGATCTATGACATATTGCTGGCTCTTATCTTCCTTCATGACAGAGGACACCTA  
ACACACAATAATGTCTGTTTATCATCTGTGTTTGTGAGTGAAGATGGACACTGGAAGCTA  
GGAGGAATGGAAACTGTTTGTAAAGTTTCTCAGGCCACACCAGAGTTTCTGAGGACTATT

## FIGURE 2QQQ

CAGTCAATAAGAGACCCAGCATCTATCCCTCCTGAAGAGATGTCTCCAGAATTCACAACT  
CTCCCAGAGTGTTCATGGACATGCCCCGGGATGCCTTTTCATTTGGAACATTGGTGGAAAAGT  
TTGCTCACAATCTTAAATGAACAGGTTTCAGCGGATGTTCTCTCCAGCTTTCAACAGAGCC  
TTGCACTCAACTTTGCTGAATCCCATTTCCAAAATGTCGGCCAGCGCTCTGCACCTTACTA  
TCTCATGACTTCTTCAGAAATGATTTTCTGGAAGTTGTGAATTTCTTGAAAAGTTTAAACA  
TTGAAGAGTGAAGAGGAGAAAACGGAATTCTTTAAATTTCTGCTGGACAGAGTCAGCTGC  
TTGTCAGAGGAATTGATAGCTTCAAGGTTGGTGCCTCTTCTGCTTAATCAGTTGGTGT  
GCAGAGCCAGTGGCTGTTAAGAGTTTTCTTCCTTATCTGCTTGGCCCCAAAAAGATCAT  
GCGCAGGGAGAAAACCTTGCTTGCTCTCACCAGCCCTGTTCCAGTCACGGGTGATCCCC  
GTGCTTCTCCAGTTGTTTGAAGTTCATGAAGAGCATGTGCGGATGGTGTCTGTCTCAC  
ATCGAGGCCTACGTGGAGCACTTCACTCAGGAGCAGCTGAAGAAAGTCATCTTGCCACAG  
GTTTTGCTGGGCCTGCGTGATACTAGCGATTCCATTGTGGCAATTACTCTGCATAGCCTA  
GCAGTGCTGGTCTCTCTGCTTGGACCAGAGGTGGTGTGGGAGGAGAACGAACCAAGATC  
TTCAAACGCACTGCCCCAAGTTTTACTAAAAATACTGACCTTTCTCTAGAAGGCGATCCA  
TTTTCTCAGCCTATTAAATTTCCCATAAATGGACTCTCAGATGTAAAAAATACTTCGGAG  
GACAGTGAAAACCTTCCCATCAAGTTCTAAAAAGTCTGAGGAGTGGCCTGACTGGAGTGAA  
CCTGAGGAGCCTGAAAATCAAACGTCAACATACAGATTTGGCCTAGAGAACCTTGTGAT  
GATGTCAAGTCCCAGTGCCTACCTTGGATGTGGAAGAGTCATCTTGGGATGACTGCGAG  
CCCAGCAGCTTAGATACTAAAGTAAACCCAGGAGGTGGAATCACTGCTACAAAACCTGTT  
ACCTCAGGGGAGCAGAAAGCCTATTCTTGCTTTGCTTTCACTCACTGAAGAGTCTATGCCT  
TGGAAATCAAGCTTACCCCAAAAGATTAGCCTTGTACAAAGGGGGGATGACGCAGACCAA  
ATCGAGCCGCCAAAAGTGTTCATCACAAAGAAAGGCCCTTAAGGTTCCATCAGAACTTGGT  
TTAGGAGAGGAATTCACCATTCAAGTAAAAAGAAGCCAGTAAAGATCCTGAGATGGAT  
TGGTTTGCTGATATGATCCCAGAAATTAAGCCTTCTGCTGCTTTTCTTATATTACCTGAA  
CTGAGGACAGAAATGGTCCCAAAAAGGATGATGTCTCCCCAGTGATGCAGTTTTCTCA  
AAATTTGCTGCAGCAGAAATTACTGAGGGAGAGGCTGAAGGCTGGGAAGAAGAAGGGGAG  
CTGAACTGGGAAGATAATAACTGGTGA

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AGCGGCCGCGGGGGCGGCGGAGGATATGGAGTAAAGCCAGAGTCAGTGGCCAGGCACGAA  
GGCAGAGCAGGAACAGCCAGGAGGCGTTTATTAGGGGGGCGGGGGGAAAGAGCCCCAGCA  
CCGCCCCCTCTGGAAGAAGGAAGAGGTAACATACTACCCAATATTGCAGCCATGGAGT  
CCATGCTTAATAAATTGAAGAGTACTGTTACAAAAGTCACAGCTGATGTCAGTAGTGCGG  
TAATGGGAATTCCTGTCACTAGAGAATTTGATGTTGGTTCGACACATTGCCAGTGGTTGCA  
ATGGGCTAGCTTGGGAAGATTTTAAATGGCACAAAAAGTCAACAAAGCAGGAAGTGGCAG  
TTTTTGTCTTTGATAAAAACTGATTGACAAGTATCAAAAATTTGAAAAGGATCAAATCA  
TTGATTCTCTAAAACGAGGAGTCCAACAGTTAACTCGGCTTCGACACCCTCGACTTCTTA  
CTGTCCAGCATCCTTTAGAAGAATCCAGGGATTGCTTGGCATTTTGTACAGAACCAGTTT  
TTGCCAGTTTAGCCAATGTTCTTGGTAACTGGGAAAATCTACCTTCCCCCTATATCTCCAG  
ACATTAAGGATTATAAACTTTATGATGTAGAAACCAAATATGGTTTGCTTCAGGTTTCTG  
AAGGATTGTCACTTCTTGATAGCAGTGTGAAAATGGTGCATGGAAATATCACTCCTGAAA  
ATATAATTTTGAATAAAAAGTGGAGCCTGGAAAATAATGGGTTTTGATTTTTGTGTATCAT  
CAACCAATCCTTCTGAACAAGAGCCTAAATTTCTTGTAAAGAATGGGACCCAAATTTAC  
CTTCATTGTGTCTTCCAAATCCTGAATATTTGGCTCCTGAATACATACTTTCTGTGAGCT  
GTGAAACAGCCAGTGATATGTATTCTTTAGGAACTGTTATGTATGCTGTATTTAATAAAG  
GGAAACCTATATTTGAAGTCAACAAGCAAGATATTTACAAGAGTTTCAGTAGGCAGTTGG  
ATCAGTTGAGTCGTTTAGGATCTAGTTCACTTACAAATATACCTGAGGAAGTTCGTGAAC  
ATGTAAAGCTACTGTTAAATGTAACCTCCGACTGTAAGACCAGATGCAGATCAAATGACAA  
AGATTCCCTTCTTTGATGATGTTGGTGCAGTAACACTGCAATATTTTGATACCTTATTCC  
AAAGAGATAATCTTCAGAAATCACAGTTTTTCAAAGGACTGCCAAAGSTTCTACCAAAAC

## FIGURE 2RRR

TGCCCAAGCGTGTTCATTGTGTCAGAGAATTTTGCCTTGTTTGAAGTTCAGAAATTTGTAAACC  
CTGACATGCTACCTTTTGTGTTTGCCTAATGTTCTACTTATTGCTGAGGAATGCACCAAAG  
AAGAATATGTCAAATTAATTCTTCTGAACTTGGCCCTGTGTTTAAAGCAGCAGGAGCCAA  
TCCAGATTTTGTAAATTTTCTACAAAAAATGATTTGCTACTAACC AAAACCCCTCTG  
ATGAGATAAAGAACAGTGTCTACCCATGTTTTACAGAGCACTAGAAGCTCCTTCCATTC  
AGATCCAGGAGCTCTGTCTAAACATCATTTCCAACCTTTGCAAATCTTATAGACTACCCAT  
CCATGAAAAACGCTTTGATACCAAGAATTAAAAATGCTTGCTACAAACATCTTCCCTTGC  
GGTTCGTGTAAATTCATTAAACAACATTGGAGCAGACCTTCTGACTGGCAGTGAGTCCG

SEQ ID NO: 88\_AA278842\_H

GGCGCGCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCCCCGGCTCGGGCGGCGCGGAG  
GACCCGGAGCTAAGGCGCCCGAACCCGCGGCGGCGGTGGGGACGATGTGGTTCTTTGCC  
GGGACCCGGTCCGGGACTTTCCGTTTCGAGCTCATCCCGGAGCCCCCAGAGGGCGGCCTGC  
CCGGGCCCTGGGCCCTGCACCGCGGCCGCAAGAAGGCCACAGGCAGCCCCGTGTCCATCT  
TCGTCTATGATGTGAAGCCTGGCGCGGAAGAGCAGACCCAGGTGGCCAAAGCTGCCTTCA  
AGCGCTTCAAACTCTACGGCACCCCCAACATCCTGGCTTACATCGATGGACTGGAGACAG  
AAAAATGCCTCCACGTCTGTGACAGAGGCTGTGACCCCGTTGGGAATATACCTCAAGGCGA  
GAGTGGAGGCTGGTGGCCTGAAGGAGCTGGAGATCTCCTGGGGGCTACACCAGATCGTGA  
AAGCCCTCAGCTTCTTGGTCAACGACTGCAGCCTCATCCACAACAATGTCTGCATGGCCG  
CCGTGTTCGTGGACCGAGCTGGCGAGTGGAAGCTTGGGGGCTGGACTACATGTATTCGG  
CCCAGGGCAACGGTGGGGGACCTCCCCGCAAGGGGATCCCCGAGCTTGAGCAGTATGACC  
CCCCGGAGTTGGCTGACAGCAGTGGCAGAGTGGTCAGAGAGAAGTGGTCAGCAGACATGT  
GGCGCTTGGGCTGCCTCATTTGGGAAGTCTTCAATGGGCCCCCTACCTCGGGCAGCAGCCC  
TACGCAACCCTGGGAAGATCCCCAAAACGCTGGTGGCCCCATTACTGTGAGCTGGTGGGAG  
CAAACCCCAAGGTGCGTCCCAACCCAGCCCGCTTCTTGCAGAACTGCCGGGCACCTGGTG  
GCTTCATGAGCAACCGCTTTGTAGAAACCAACCTCTTCTGAGGAGATTCAGATCAAAG  
AGCCAGCCGAGAAGCAAAAATCTTCCAGGAGCTGAGCAAGAGCCTGGACGCATTCCTTG  
AGGATTTCTGTGCGCACAAAGGTGCTGCCCCAGCTGCTGACCGCCTTCGAGTTCCGCAATG  
CTGGGGCCGTGTCTCTACGCCCCCTCTTCAAGGTGGGCAAGTTCTTGAGCGCTGAGGAGT  
ATCAGCAGAAGATCATCCCTGTGGTGGTCAAGATGTTCTCATCCACTGACCGGGCCATGC  
GCATCCGCTCCTGCAGCAGATGGAGCAGTTCATCCAGTACCTTGACGAGCCAACAGTCA  
ACACCCAGATCTTCCCCCACGTCTGTACATGGCTTCTTGACACCAACCCTGCCATCCGGG  
AGCAGACGGTCAAGTCCATGCTGCTCCTGGCCCCAAAGCTGAACGAGGCCAACCTCAATG  
TGGAGCTGATGAAGCACTTTGCACGGCTACAGGCCAAGGATGAACAGGGCCCCATCCGCT  
GCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCAGTGCTAGCACCAGACACA  
GGGTCTTTACCTCTGCCTTCAGCCGAGCCACTAGGGACCCGTTTGCACCGTCCCGGGTTG  
CGGGTGCTCTGGGCTTTGCTGCCACCCACAACCTCTACTCAATGAACGACTGTGCCCAGA  
AGATCCTGCCTGTGCTCTGCGGTCTCACTGTAGATCCTGAGAAATCCGTGCGAGACCAGG  
CCTTCAAGGCCATTCCGAGCTTCTGTCCAAATTGGAGTCTGTGTGCGGAGGACCCGACCC  
AGCTGGAGGAAGTGGAGAAGGATGTCCATGCAGCCTCCAGCCCTGGCATGGGAGGAGCCG  
CAGCTAGCTGGGCAGGCTGGGCGGTGACCGGGGTCTCCTCACTCACCTCCAAGCTGATCC  
GTTTCGACCCCAACCACTGCCCCAACAGAAACCAACATTTCCCCAAAGACCCACGCCTGAAG  
GAGTTCTTGCCCCAGCCCCCACCCTGTTCTGCCCCCTACAACCTCAGGCCACTGGG  
AGACGCAGGAGGAGGACAAGGACACAGCAGAGGACAGCAGCACTGCTGACAGATGGGACG  
ACGAAGACTGGGGCAGCCTGGAGCAGGAGGCCGAGTCTGTGCTGGCCAGCAGGACGACT  
GGAGCACC GGGGGCAAGTGAGCCGTGCTAGTCAAGTCAAGCAACTCCGACCACAAATCCT  
CCAAATCCCCAGAGTCCGACTGGAGCAGCTGGGAAGCTGAGGGCTCCTGGGAACAGGGTT  
GGCAGGAGCCAAGCTCCGAGGAGCCACCTCCTGACGGTACACGGCTGGCCAGCGAGTATA  
ACTGGGGTGGCCAGAGTCCAGCGACAAGGGCGACCCCTTGGCTACCTGTCTGCACGTG  
CCAGCACCCAGCCGAGGCCAGACTCTTGGGGTGAGGACAACTGGGAGGGCCTCGAGACTG



## FIGURE 2SSS

ACAGTCGACAGGTCAAGGCTGAGCTGGCCCGGAAGAAGCGCGAGGAGCGGCGGCGGGAGA  
TGGAGGCCAAACGCGCCGAGAGGAAGGTGGCCAAGGGCCCCATGAAGCTGGGAGCCCGGA  
AGCTGGACTGAACCGTGGCGGTGGCCCTTCCCGGCTGCGGAGAGCCCGCCCCACAGATGT  
ATTTATTGTACAAACCATGTGAGCCCGGCCGCCAGCCAGGCCATCTCACGTGTACATA  
ATCAGAGCCACAATAAATTCTATTTTAC

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ATGGCCTTCATGGAGAAGCCGCCAGCCGGCAAGGTGCTGCTGGACGACACGGTGCCGCTG  
ACAGCAGCCATCGAGGCGAGCCAGAGCCTGCAGTCCCACACGGAATATATTATTTCGAGTG  
CAAGGAGGAATTTCTGTGGAAAACAGCTGGCAGATTGTTAGAAGATACAGTGACTTTGAT  
TTGCTTAACAACAGCTTACAGATTGCAGGCCTAAGTCTACCTCTTCCCTCCCAAAAATTG  
ATTGGTAACATGGATCGTGAATTCATAGCTGAAAGGCAGAAAGGTCTTCAGAACTATCTC  
AACGTGATCACAAACAATCATATCTTGTCTAATTGTGAGCTGGTTAAGAAGTTTTTAGAT  
CCAAACAACATATTCCGCAAACTATACTGAGATTGCCTTGCAACAGGTTTCCATGTTCTTC  
CGATCAGAGCCAAAGTGGGAGGTGGTGGAAACCTTTGAAAGACATAGGTTGGAGAATAAGG  
AAGAAATATTTCTTGATGAAGATTAAAAATCAGCCAAAGGAACGGCTAGTGTTAAGCTGG  
GCTGACCTTGCGCCAGACAAGTATTTGTGAGATAAAGATTTTCAGTGTCTAATCAAACCTT  
CTGCCTTCTTGTTTGCACCCCTTACATCTATCGGGTTACCTTTGCCACAGCTAATGAATCC  
TCAGCGTTGCTAATTAGGATGTTTAACGAAAAGGGAACATTGAAGGATCTGATCTACAAG  
GCAAAACCAAAAGACCCATTTCTAAAGAAGTACTGCAACCCTAAGAAGATTTCAGGGCCTG  
GAACTCCAGCAAATAAAAACATATGGACGGCAAATATTAGAGGTACTGAAGTTTCTTCAT  
GACAAGGGATTCCCTTATGGGCATCTTCACGCCTCCAATGTGATGCTCGATGGGGACACT  
TGCCGGCTGCTGGACCTTGAGAATTCCTTATTGGGCCTGCCTTCTTCTACCGATCTTAT  
TTTTCACAAATTCAGGAAAATCAATACATTGGAAAGTGTGGATGTCCACTGCTTTGGCCAC  
TTACTGTATGAAATGACTTATGGACGACCGCCAGACTCGGTGCCTGTGGACTCCTTCCCT  
CCTGCCCCGTCATGGCTGTGGTGGCCGTGTTGGAGTCTACGCTGTCTTGTGAAGCCTGT  
AAAAATGGCATGCCTACCATCTCCCGGCTCTTACAGATGCCATTATTCAGCGATGTTTTTA  
CTAACCACTTCTGAAAAACCAAGTTTAAGATCCCTACAAAGTTAAAAGAGGCATTGAGA  
ATTGCCAAAGAATGTATAGAGAAGAGACTAATTGAGGAACAGAAACAGATTCACCAGCAT  
CGAAGACTGACAAGAGCTCAGTCCCACCATGGATCTGAGGAGGAAAGAAAAAAGAAAG  
ATTTTAGCTCGAAAGAAGTCAAAACGATCTGCTCTTGAAAATAGTGAAGAGCATTTCAGCG  
AAGTACAGCAACTCCAATAATTCAGCAGGATCTGGGGCCAGCTCACCTCTCACGTCCCCG  
TCATCGCCAACTCCACCCTCTACATCAGGGATATCTGCATTACCTCCTACCTCCTCCACCT  
CCACCACCACAGCAGCTCCCTTGCTCCTGCGAGCACCGAGGCACCTGCCAGCTCTCG  
TCTCAGGCTGTGAATGGCATGAGCCGAGGGGCCTTGCTCAGCTCCATCCAGAATTTCCAA  
AAAGGAACTTTGAGGAAAGCCAAACCTGTGATCACAGTGCTCCGAAGATCGGCTGAAGCT  
TCCTGTTTACACTTGAGGGGAAAAGTTCTTTTTTATTCCTACTACCCCTACCCCCAAC  
TACCCTCTTCTGGGAAAGTAATTGCTGAGCCAGTACAGCCACAAACAGTACTATTTTGC  
AGATGCTCATGTAAGCAGCTTTTCGAGAGAAATAATTCTTTAAGCAGAATAAAGTTAGGC  
TGGCATGCAAAAAAAAAAAAAAAAAAAAAA

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ATGAGCGCCAGCACGGGCGGTGGTGGGGACAGCGGCGGCAGCGGCGGCAGTAGCAGCAGC  
TCACAGGCCTCCTGCGGGCCCGAGTCTTCCGGGCTCCGAAGTAGCCCTGGCCACACCGGTG  
CCTCAGATGCTGCAGGGCCTTCTGGGCTCCGACGACGAGGAACAGGAAGACCCCAAAGAC  
TACTGCAAGGGCGGCTACCACCTGTGAAGATCGGCGACGTGTTCAATGGGCGGTACCA  
GTGGTGGCAAACCTGGGCTGGGGCCACTTCTCCACCGTCTGGCTCTGCTGGGACATCCAG  
CGCAAGCGCTTTGTGGCCCTCAAAGTGGTGAAGAGTGCGGGGCATTACACGGAGACAGCT  
GTGGATGAGATCAAGCTCCTGAAATGTGTCCGGGACAGCGACCCAGTGACCCCAAAGA  
GAGACCATTGTCCAGCTCATTGATGACTTCAGGATCTCAGGAGTCAATGGAGTCCATGTG

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## FIGURE 2TTT

TGCATGGTGCTGGAGSTGCTGGGGCCACCAGCTCCTCAAATGGATCATCAAGTCCAACTAC  
CAGGGCCTGCCCGTGCCCTGCGTGAAGAGCATCGTGAGGCAGGTGCTGCACGGCCTGGAC  
TACCTCCACACCAAGTGAAGATCATCCACACGGACATCAAGCCCGAGAACATCTTGCTG  
TGTGTGGGGGAAGCTTACATCAGGCGCCTGGCTGCCGAGGCCACGGAGTGGCAACAGGCA  
GGGCGCGCCGCCCCCTCCCGCTCCATACTCAGCACTGCCCCCAGGAGGTCTTGACCGGT  
AAGCTGTCCAAAAACAAGAGGAAGAAGATGAGGCGCAAACGGAAACAGCAGAAGCGGCTG  
CTGGAGGAGCGCTGCGGGACCTGCAGAGSCTGGAGGCCATGGAGGCTGCCACCCAGGCT  
GAGGACTCTGGCTTGAGACTAGACGGGGGCAGCGGCTCCACATCCTCTTCAGGCTTCTCC  
GGCTCCCTCTTCTCTCCTGCCTCCTGCTCCATCCTCTCCGGCTCGTCCAATCAGCGAGAG  
ACCGGGGGCCTCCTGTGCCTAGCACACCATTGCGGTGCCTCGAACCTCCTGGTGAACCCC  
CTGGAGCCCCAAAATGCAGATAAGATCAAGATCAAGATCGCAGACCTGGGCAACGCCTGC  
TGGGTGCACAAGCACTTCACGGAAGACATCCAGACTCGGCAGTACCGGGCCGTCGAGGTG  
CTGATCGGCGCCGAATACGGCCCCCGGCAGACATCTGGAGCACAGCCTGCATGGCCTTC  
GAGCTGGCCACTGGTGACTACCTGTTTCGAGCCGCATTCTGGAGAAGACTACAGTCGTGAT  
GAGGACCACATCGCTCACATAGTGGAGCTTCTGGGGGACATCCCCCAGCCTTCGCCCTC  
TCAGGCCGCTATTCCCGGGAGTTCTTCAACCGGAGAGGAGAGCTGCGGCACATCCACAAT  
CTCAAGCACTGGGGCCTGTACGAGGTACTCATGGAAAAGTACGAGTGGCCCCCTAGAGCAG  
GCCACACAGTTCAGCGCCTTTCTGCTGCCCATGATGGAGTACATCCCCGAAAAGCGGGCC  
AGTGCCGCTGACTGCCTCCAGCACCCCTGGCTCAACCCCTAG

SEQ ID NO: 91\_SGK022\_H

TCTGGCCCTGTCCCTCCCCACCCCGCCGCTGTGTCCAGACAGAGAATGTTCTAACGCT  
GGGGGCGGCTGCGGATGAAGTCCTTGGGGAGAAAAGGAGCAGGCCAAGGGCGATGGTGGA  
GTAGAGCTGCCTCTCAGAGGCAGCATGAGCTGAGAGGGTGATAGGAAGGCGGCGCTAGAC  
AGCATGGAGGACTTTCTGCTCTCCAATGGGTACCAGCTGGGCAAGACCATTGGGGAAAGG  
ACCTACTCAAAAGTCAAAGAAGCATTTTCCAAAAAACACCAAAGAAAAGTGGCAATTAAA  
GTTATAGACAAGATGGGAGGGCCATCAGAGTTTATCCAGAGATTCCCTCCCTCGGGAGCTC  
CAAATCGTCCGTACCCTGGACCACAAGAACATCATCCAGGTGTATGAGATGCTGGAGTCT  
GCCGACGGGAAAATCTGCCTGGTGATGGAGCTCGCTGAGGGAGGGGATGTCTTTGACTGC  
GTGCTGAATGGGGGGCCACTGCCTGAAAGCCGGGCCAAGGCCCTCTTCCGTCAGATGGTT  
GAGGCCATCCGCTACTGCCATGGCTGTGGTGTGGCCACCGGGACCTCAAATGTGAGAAC  
GCCTTGTTGCAGGGCTTCAACCTGAAGCTGACTGACTTTGGCTTTGCCAAGGTGTTGCC  
AAGTCACACCGGGAGCTGAGCCAGACCTTCTGCGGCAGTACAGCCTATGCTGCCCCCGAG  
GTGCTGCAGGGCATTCCCCACGATAGCAAAAAGGTGATGTCTGGAGCATGGGTGTGGTC  
CTGTATGTATGCTCTGTGCCAGCCTACCTTTTGACGACACAGACATCCCCAAGATGCTG  
TGGCAGCAGCAGAAGGGGGTGTCTTCCCCACTCATCTGAGCATCTCGGCCGATTGCCAG  
GACCTGCTCAAGAGGCTCCTGGAACCCGATATGATCCTCCGGCCTTCAATTGAAGAAGTT  
AGTTGGCATCCATGGCTAGCAAGCACTTGATAAAAGCAATGGCAAGTGCTCTCCAATAAA  
GTAGGGGGAGAAAGCAA

SEQ ID NO: 92\_AA060026\_M SGK022\_M

CAGACGGAGAATGTTCTAGCCCTGGAGGCAGCTGTGAATGAAGTCCTTGGGGGGGAAAAGA  
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GTGACAAGAAGGAGGCGCTACACAGCATGGAGGACTTTCTACTCTCCAATGGGTATCAGC  
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ATCAAAGAAAAGTGGCAATTAAAATTATAGACAAGATGGGAGGGGCCAGAAGAGTTTATCC  
AGAGATTCCCTGCCTCGTGAGCTCCAGATTGTCCGTACCCTGGACCACAAAACATCATCC  
AGGTGTATGAGATGCTGGAGTCAGCAGATGGAAAAATCTACCTGGTGATGGAACTGGCTG  
AGGGAGGGGATGTCTTTGACTGTGTGCTGAACGGAGGGGCCACTTCCCGAGAGCCGGGGCA  
AGGCCCTCTTCCGCCAGATGGTTGAGGCTATTGCTATTGCCATGGCTGTGGCGTGGCCC

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## FIGURE 2UUU

ACCGGGACCTTAAGTGTGAGAACGCCTTGTTGCAGGGCTTCAACCTGAAGCTGACCGACT  
TTGGCTTTGCCAAGGTGCTACCCAAGTCACGCAGGGAGCTGAGCCAGACCTTCTGTGGCA  
GCACAGCCTATGCCGCCCTGAGGTGCTACAGGGCATACCCCATGATAGCAAGAAAGGTG  
ATGTCTGGAGCATGGGTGTGGTCCTGTATGTAATGCTCTGTGCAAGTCTACCTTTTGATG  
ACACAGATATCCCCAAGATGCTGTGGCAGCAGCAGAAGGGGGTGTCTTCCCCACTCATT  
TGGGCATCTCAACCGAATGCCAGGACCTGCTCAAGCGGCTCCTGGAACCAGACATGATAC  
TCCGGCCTTCAATCGAAGAAGTTAGTTGGCACCCATGGCTAGCAAGCACTTGATAAAAGC  
AATGGCAAGTCTCCCCAATAAAGTAGGGGGAGAAAGCAAAGT

SEQ ID NO: 93\_AA399669\_H

CTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCCACTTCATTCTCAA  
GTTTTGTGGCCAACGATGGATAGGAGGTGGATTGTGATGTATTTCGGAACATGGGACCTTG  
AGGAGTTCCGTAACCAAAAGGAGAAAGTAACAACAGCCAGTGGAGACAAAAAGAACTGCT  
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GTGACTATATAGGCAAGCATTGTTGGGGACCTACTTCACTTTGATACCCTAGCCTTCAGCAG  
CTCAAGGTGTTGGCCTTTGGATAGGAGGCTTCCAAGTAGTAAAGCTCCCTGCTCTCAGCA  
AGCCCAACACCATGGGGAAGGGAGATGTCTTAGAGGCAGCACCAACCACCACAGCCTACC  
ATTCCCTCATGGATGAATATGGTTATGAGGTGGGCAAGGCCATTGGCCATGGCTCCTATG  
GGTCGGTATATGAGGCTTTCTACACAAAGCAGAAGGTTATGGTGGCAGTCAAGATCATCT  
CAAAGAAGAAGGCCTCTGATGACTATCTTAACAAGTTCCTGCCCCGTGAAATACAGGTAA  
TGAAAGTCTTGCGGCACAAGTACCTCATCAACTTCTATCGGGCCATTGAGAGCACATCTC  
GAGTATACATCATTCTGGAAGTGGCTCAGGGTGGTGATGTCCTTGAATGGATCCAGCGCT  
ACGGGGCCTGCTCTGAGCCCCTTGCTGGCAAGTGGTTCTCCCAGCTGACCCTGGGCATTG  
CCTACCTGCACAGCAAGAGCATCGTGCACCGGGACTTAAAGTTGGAGAACCTGTTGCTGG  
ACAAGTGGGAGAATGTGAAGATATCAGACTTTGGCTTTGCCAAGATGGTGCCTTCTAACC  
AGCCTGTGGGTGTAGCCCTKCTTACCGCCAAGTGAAGTGCCTTTTCCACCTCAGCCAGA  
CTTACTGTGGCAGCTTTGCTTACGCTTGCCCAGAGATCTTACGAGGCTTGCCCTACAACC  
CTTTCCTGTCTGACACCTGGAGCATGGGCGTCATCCTTTACACTCTAGTGGTCGCCCATC  
TGCCCTTTGATGACACCAATCTCAAAAAGCTGCTAAGAGAGACTCAGAAGGAGGTCACTT  
TCCCAGCTAACCATAACCATCTCCCAGGAGTGCAAGGTCCAAGTGCCTATTGCCTGTGTGG  
CACAATGGAGAAAAAAGTCAAGGCAAGACCTCTCTCTCCCCTGCTCTAGAACCCTGATCCTCC  
AGATGCTACGCCAAGCCACTAAGCGTGCCACCATTCTGGACATCATCAAGGATTCTTGGG  
TGCTCAAGTTCCAGCCTGAGCAACCCACCCATGAGATCAGGCTGCTTGAGGCCATGTGCC  
AGCTCCACAACACCACTAAACAGCACCAATCCTTGCAAATTACGACCTGAAAATGGCTGA  
GGGAGGGGGCTAAGAGAGGAGCAAAGCAGGAGGTCTTGGGCTAAAAATCTTTTTTACCAA  
AAATAAATCTAAGTCTGATTTAGTTTCATCAAAAAA

SEQ ID NO: 94\_AA758539\_H

GACCATTGACACGCCTCCGGTAGTGTAATGAGGACAATGCCTGCTGGCCACATGACGG  
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AAGGAAGAAGGGTTACATCGTAGGCATCAATCTTGGCAAGGGTTCTACGCAAAAGTCAA  
ATCTGCCTACTCTGAGCGCCTCAAGTTCAATGTGCTGTCAAGATCATCGACCGCAGGAA  
AACACCTACTGACTTTGTGGAGAGATTCTTCTCCTCGGGAGATGGACATCCTGGCAACTGT  
CAACCACGGCTCCATCATCAAGACTTACGAGATCTTTGAGACCTCTGACGGACGGATCTA  
CATCATCATGGAGCTTGGCGTCCAGGGCGACCTCCTCGAGTTCATCAAGTGCCAGGGAGC  
CCTGCATGAGGACGTGGCAGCAAGATGTTCCGACAGCTCTCCTCCGCCGTCAAGTACTG  
CCACGACCTGGACATCGTCCACCGGGACCTCAAGTGGGAGAACCTTCTCCTCGACAAGGA  
CTTCAACATCAAGCTGTCTGACTTTGGCTTCTCCAAGCGCTGCCTGGGGACAGCAATGG  
GCGCATCATCCTCAGCAAGACCTTCTGCGGGTGGCAGCATATGCAGCCCCCGAGGTGCT  
GCAGAGCATCCCCTACCAGCCCAAGGTGTATGACATCTGGAGCCTGGGCGTGATCCTGTA

## FIGURE 2VVV

CATCATGGTCTGCGGCTCCATGCCCTATGACGACTCCGACATCAGGAAGATGCTGCGTAT  
CCAGAAGGAGCACCGTGTGGACTTCCCGCGCTCCAAGAACCTGACCTGCGAGTGAAGGA  
CCTCATCTACCGCATGCTGCAGCCCCGACGTACGCCAGCGGCTCCACATCGATGAGATCCT  
CAGCCACTCGTGGCTGCAGCCCCCAAGCCCAAAGCCACGTCTTCTGCCTCCTTCAAGAG  
GGAGGGGGGAGGGCAAGTACCGCGCTGAGTGCAAACCTGGACACCAAGACAGGCTTGAGGCG  
CGACCACCGGCCCGACCACAAGCTTGGAGCCAAAACCCAGCACCGGCTGCTGGTGGTGCC  
CGAGAACGAGAACAGGATGGAGGACAGGCTGGCCGAGACCTCCAGGGCCAAAGACCATCA  
CATCTCCGGAGCTGAGGTGGGGAAAGCAAGCACCTAGCATGACAATGGCCCCGTTGTGTG  
TGGTGGGGGTGCGGGTTGGGGGGCATGGTGAGTCGGCCTTCACGTAAACTAAGTAGGCA  
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SEQ ID NO: 95\_AA883975\_H

ATGTCGGGAGACAAACTTCTGAGCGAACTCGGTTATAAGCTGGGCCGCACAATTGGAGAG  
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AAGGTGGTGGACCGGCGGCGAGCGCCCCCGGACTTCGTCAACAAGTTCTTCCGCGGAGAG  
CTGTCCATCCTGCGGGGCGTGCGACACCCGCACATCGTGACGTCTTCGAGTTCATCGAG  
GTGTGCAACGGGAAACTGTACATCGTGATGGAAGCGGCCGCCACCGACCTGCTGCAAGCC  
GTGCAGCGCAACGGGCGCATCCCCGGAGTTCAGGCGCGCGACCTCTTTGCGCAGATCGCC  
GGCGCCGTGCGCTACCTGCACGATCATCACCTGGTGCACCGCGACCTCAAGTGCGAAAAC  
GTGCTGCTGAGCCCCGACGAGCGCCGCGTCAAGCTCACCGACTTCGGCTTCGGCCGCCAG  
GCCCCATGGCTACCCAGACCTGAGCACCACTACTGCGGCTCAGCCGCTACGCGTCACCC  
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GTGCTCTACGTCTATGGTCACCGGGTGCATGCCCTTCGACGACTCGGACATCGCCGGCCTG  
CCCCGGCGCCAGAAACGCGGCGTGCTCTATCCCCAAGGCCTCGAGCTGTCCGAGCGCTGC  
AAGGCCCTGATCGCCGAGCTGCTGCAGTTCAGCCCCGTCCGCCAGGCCCTCCGCGGGCCAG  
GTAGCGCGCAACTGCTGGCTGCGCGCCGGGACTCCGGCTAG

SEQ ID NO: 96\_AA905446\_H

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GGACAAATCAGGCCTTATAATTTGTGATTCTGTGGCTTTGTCTAAAAGTCCATAAAGCAC  
CTTGATATCCAGTCTCACAGACTGCTCACAACAGTCCACAAGGCTGGTGGGGAGTGCTTC  
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CAGCTAGACACACTTAAGACCATTAAGAAAGCCAAGAAATAAGACCCAGACAAGGTGGGC  
AGAAGTTGGAAGGCAGGAGACAGGTGTGAGGAGGTGGGCCTTTCTGATCTGCCAGCCCAT  
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CGTCCGTACCCTGGACCACAAGAACATCATCCAGGTGTATGAGATGCTGGAGTCTGCCGA  
CGGGAAAATCTGCCTGGTGATGGAGCTCGCTGAGGGAGGGGATGTCTTTGACTGCGTGCT  
GAATGGGGGGCCACTGCCTGAAAGCCGGGCCAAGGCCCTCTTCCGTGAGATGGTTGAGGC  
CATCCGCTACTGCCATGGCTGTGGTGTGGCCCACCGGGACCTCAAATGTGAGAACGCCTT  
GTTGCAGGGCTTCAACCTGAAGCTGACTGACTTTGGCTTTGCCAAGGTGTTGCCCAAGTC  
ACACCGGGAGCTGAGCCAGACCTTCTGCGGCAGTACAGCCTATGCTGCCCCCGAGGTGCT  
GCAGGGCATTTCCNNCAAGATGCTGTGGCAGCAGCAGAAGGGGGTGTCTTCCCCACTCA  
TCTGAGCATCTCGGCCGATTGCCAGGACCTGCTCAAGAGGCTCCTGGAACCCGATATGAT  
CCTCCGGCCTTCAATTGAAGAAGTTAGTTGGCATCCATGGCTAGCAAGCACTTGATAAAA  
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## FIGURE 2WWW

SEQ ID NO: 97\_H29974\_H

TTACAGCCTGTTGGCGGAGATCGGGCGCGGCAGCTACGGCGTGGTTTATGAGGCAGTGGC  
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GGAGCTGGCGCTGGCTGAATTTCTGGGCCCTCACCAGCCTCAAGCGGCGCCACCAGAACGT  
CGTGCAAGTTTGGAGAGTGCCTCCTGCAGCGCAATGGGTAGCCCAGCGCATGAGTCAAGG  
CAACAAGAGCTCGCAGCTTTACCTGCGCCTGGTGGAGACCTCGCTGAAAGGAGAAAGGAT  
CCTGGGTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTTCATGGAGTTCTGTGAAGGTGG  
AGACCTGAATCAGTATGTCCTGTCCCGAGAGCCAGACCCAGCCACCAACAAAAGTTTCAT  
GCTACAGCTGACGAGCGCCATTGCCTTCCTGCACAAAAACCATATTGTGCACAGGGACCT  
GAAGCCAGACAACATCCTCATCACAGAGCGGTCTGGCACCCCCATCCTCAAAGTGGCCGA  
CTTTGGACTAAGCAAGGTCTGTGCTGGGCTGGCACCCCCGAGGCAAAGAGGGCAATCAAGA  
CAACAAAATGTGAATGTGAATAAGTACTGGCTGTCTCAGCCTGCGGTTTCGGACTTCTA  
CATGGCTCCTGAAGTCTGGGAGGGACACTACACAGCCAAGGCGGACATCTTTGCCCTGGG  
CATTATCATCTGGGCAATGATAGAAAGAATCACTTTTATTGACTCTGAGACCAAGAAGGA  
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AGAAAACCCAAAGATGGAGTTGCACATCCCCCAAAAACGCAGGACTTCCATGTCTGAGGG  
GATCAAGCAGCTCTTGAAAGATATGTTAGCTGCTAACCACAGGACCGGCCTGATGCCTT  
TGAAGTTGAAACCAGAATGGACCAGGTCACATGTGCTGCTTAAAATTTCAGGGCTAAGCAT  
TTTGGGTGATTTTAACTAGGTTCGATTCCCTCGGGACCCACAGTCTCACCACGTCTCCTCC  
AGAGGACGGCAGAGGGTACAGGTGGTGGCCTGGCCGGTTGGCGATCTCCCGACAGCTGGA  
TCCGGCAATGTGAAGCTTTTGTGGGTTTCCCCGCTTCTTTTTTAGTTTTGCTTTATTTN  
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TCTGGAACGGGGCGTGAGGANACAAGGAGCCTCTGGGCCACNCCTCCCTACCAGATGCAG  
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GAGGTGAAGAACCGCC

SEQ ID NO: 98\_AA498104\_M H29974\_M

CCGTTGCTGCTCCCCCGCCCCCGCAGCCATGGAAACGGGGAAAGAGAACGGAGCCCCG  
AGAGGGACAAAAAGCCCGGAGCGGAAAGGCGAAGCCCAGTCCAGCGGGTACTGTGCGAG  
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AGCCTCTTGGCGGAGATCGGGCGCGGCAGCTACGGCGTGGTTTTATGAGGCTGTGGCTGGG  
CGCAGTGGGGCCAGGGTGGCAGTCAAGAAGATCCGCTGCGACGCTCCCGAGAACGTGGAG  
TTGGCACTAGCAGAATTCTGGGCCCTCACCAGTCTCAAGCGGCGGCACCAGAATATCGTG  
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AAGAACTCACAGCTTTACCTGCGCCTGGTGGAGACCTCGCTCAAAGGAGAAAGGATCCTG  
GGCTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTTCATGGAGTACTGTGAAGGTGGAGAC  
CTCAATCAGTATGTCCTGTCCCGGAGACCTGACCCAGCCACCAACAAAAGTTTCATGCTA  
CAGCTTACAAGCGCCATTGCCTTCCTGCATAAAAACCATATCGTGCACAGGGACCTAAAG  
CCAGACAACATCCTGATCACAGAGCGGTCTGGCACCCCCATCCTCAAGGTGGCAGACTTT  
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ATCATCTGGGCAATGATAGAAAGAATTACCTTTATTGACTCTGAAACCAAGAAGGAGCTC  
CTGGGGACCTACATTAAGCAAGGGACTGAGATCGTCCCTGTTGGTGAGGCGCTGCTAGAA  
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## FIGURE 2XXX

AAGCAGCTCTTGAAAGACATGTTAGCTGCTAACCCACAGGACCGACCTGATGCTTTTGAA  
CTTGAAACCCGAATGGACCAGGTACATGTGCTGCTTAAACTCCAGGGCTGAACGTCTTG  
GGTGTTTTTTAAACTAGGTTCGATCCTTCGGGACCCACAGTCTCATCGTGTCTCGGACAGGA  
TGGCAGAGGGTACAGSTGGTGGTGATCTCCTGACAGCTGGACCTCCCACAATGTGAAGCT  
CACGCTTGGGCTGCCCCACTCTACCCTTCTCTTTCTCCTTCAGTAGAATAATAATTGTTTT  
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SEQ ID NO: 99\_AA215311\_H

CGRCCGCGCTACGAAAGCCGGAGGGGGGCGGGGCGCTCGGCGTAAGGGGGTGTGTCCGC  
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GAAACCTCGACCTTGAAGATGGTGAGTAGCCAGCCAAAGTACGATCTAATACGGGAGGTA  
GGCCGAGGTAGTTACGGTGTGTGTATGAAGCAGTCATCAGAAAGACCTCTGCACGGGTG  
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TGGGCACTAAGCAGTATCAAGAGCCAACATCCAAATGTGATTCACTTGGAGGAATGCATC  
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CAGCTTGTAGAACTTCATTAAAAGGAGAAATTGCCCTTGATCCCAGAAGCGCCTATTAT  
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GAGTCCAGTTTTCTGGAAATATGTCTTTAAGTATTTTAGACATTCCTCGTCAGTATTAGG  
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CCTAATGAAATCATATTAAGTNGTTTTCTCTNNTTTTTTTTGTAAATATACAGCTTTTTTTT  
TAAGGCATCATTTTCGAGGGTCTAAAATTATCTGGTAAACAAATGAAATTAAGTGATCC  
AAAGCTGCTGAAGTATGTTTGAAGTCTCCAGTGCCCTATAGCTGCAAGAGTTGAATTAGT  
CATGCAGTCATATGGCAGCAGGTTGGTGATT

SEQ ID NO: 100\_AA018361\_H

GCGGGGCGCTCCGTATCCCCACGTGGGCGCTGCAGGAACTGGCGGGGCGCGTGACCCGGCG  
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GCAACCCGCGCGGAACCGCGCGCGCGAGCGAGGSAAGCGCGCGCGCGGCGCGCAGGCGCGCGG  
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GGGCAGCGGCACGTACGCCACGGTGTACAAAGGCTACGCCAAGAAGGACACTCGTGAAGT

## FIGURE 2YYY

GGTAGCCATAAAGTGTGTAGCCAAGAAAAGTCTGAACAAGGCATCGGTGGAGAACCTCCT  
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TCGCTTCATCCATAACCCGAGGATTCTGCCTGAGAAGGTGGCGCGTGTCTTCATGCAGCA  
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CGCACAAACATGTCCCCGTGGGATGAGAAGCACGTGCTCCGTGGCTCCCCCTCTACAT  
GGCCCCCGAGATGGTGTGCCAGCGGCAGTATGACGCCCGCGTGGACCTCTGGTCCATGGG  
GGTCATCCTGTATGAAGCCCTCTTCGGGCAGCCCCCTTTGCCTCCAGGTCGTTCTCGGA  
GCTGGAAGAGAAGATCCGTAGCAACCGGGTCATCGAGCTCCCCTTGCGGCCCTGCTCTC  
CCGAGACTGCCGGGACCTACTGCAGCGGCTCCTGGAGCGGGACCCAGCCGTCGCATCTC  
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AGCAGCCGCCTTATCACTCTACTGCAAGGCTCTGGACTTCTTTGTACCTGCCCTGCACTA  
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CTCTGCCCCGAGACCTGCTCAGAGAGATGGCCCCGGGACAAGCCACGCCTCCTAGCTGCCCT  
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AGGCGGGAGCTGCTTCACACTGAGGTTTCAAGCCTCATGGCCCCGAGCTGAATACTTGAAG  
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CCCTGGCGAGCAGGCTTCTTGGATGGACAGTGCTGAGACCCCCATATCCCAGAGTCCCCA  
GCCTCCCTCAGGTTACTCTGCACCCACAGATGGTTTGGATGGCTGTGCTGTATACTGGAG  
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GAAGAGGGCAAGGGGGCCCCCGCAGGGTACTTCTGTGCTTGCCCTCGCCCTGCCAGCAGGC  
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TTAATCCCTCAAGCATGAAAGCTGGATCTTTTGGGGTTTAAGAAGCCCAAGCCTTGTTCC  
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CCCTCTGGGCCCCACACTAGCCACAGCGCGGGCCTTGTGCTGGAGTTTGAGCCTGGGACA  
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SEQ ID NO: 101\_AA311714\_H

TGGACCTGTCTTGAGGCAGAGGCCGAGATGCGCGCAACCGCGGGAGCAGCCAAGTGGACT  
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GATAAGTGCAGAAGGCCTGAAATAACCAACTGGGTCCGTCTCACCCGTGAAATAAAACAC  
AAGAATATTGTAACCTTTTCATGAATGGTATGAAACAAGCAACCACCTCTGGCTAGTGXAT  
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## FIGURE 2ZZZ

GGGCCTGSCACACTGAACTTTTAGCAACTTTTGCCTTGGCAAAAGTGGAAAGGTGAAAAATTTG  
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GAAATGTTTTTCAGGAAAACCTCCATTCTTCTCAGAAAGTGTTTCAGAATTAAGTGAAG  
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GTTGAGACTACAAGCTCCATTGGAATCGGGATTTTGAAGTGTCTTGTTCAACACTCCACT  
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AAACTGTATCAGCATT

SEQ ID NO: 102\_SGK384\_H

TCTTTGGCCACGCTGCTGAGGGCGCGGCAGATCCTGACGGAGCCAGAAGTGC GCGACTAC  
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SEQ ID NO: 103\_AA210451\_M SGK384\_M

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CCACCGCGGACTCTAGGCGCTGTCTCCGGGCTACTTCAGAATGGGGCGGATGAGAACT  
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## FIGURE 2AAAA

TAGACGCTTACCAGAGGGTTTTCCATTCACTCCGAGACACTGTGATGTCGCAGACGAAAG  
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ACGTAGGCCTCCTCTACGTCTGCCTGCATGTTTGAGTGTCTCTGCTCTCCTGGCAGCCCCG  
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CTTTCTACCCTACTTCTTCCCTTTCCACCCCCTAACACTAGATAGGAGAGAGGAGAGAGA  
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GTCCCCCTGTACCGGAAAGTACAAAGTCTGCTCTGGGCTTGCATGCCTGAACACTTTAAA  
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SEQ ID NO: 104\_SGK071\_2\_H

GAGGTGGTGGCTGTGCAGATGATGGTGGAAATGCATGGATGACCATTACGCCAGTCAGGCC  
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AATGAGCTCAGCTTCCAGGAGGTCAATTGAGGATAAGAGGAAGGCAAAGAAAATCATTGAC  
TCTGAGTGGATGCAGAATGTGCTGGGCCAGGTGCTGGACGCGCTGGAATACCTGCACCAT  
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CACCGGCAGATGGTGCCTGCGTCCATCACCGACATGCTGTTAGAAGGCAACGTGGCCAGC  
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TTGGCATCCTATTGTTTAGTTCCAGAGGGTTCATTATTTATGCCCCCTGGCCTTGCTCCAC  
ATGCACGACCAGTGGCTCAGCTGTGACCAGGACAGAGTCCCTGGGAAGAGAGACTTTGCC  
TCCCTGGGGAAACTAGGGAAGCTGTTGGGGCCCCATCCCAAAGGGTCTGCCGTGGCCCCCG  
GAGCTGGTGGAGGTGGTGGTCACGACCATGGAGCTACATGACAGGGTCTCTCGATGTCCAG  
CTGTGTGCCTGCTCCCTGCTGCTGCACCTCCTGGGCCAAGCGCTGGTGCACCACCCGGAA  
GCCAAGGCTCCCTGCAACCAAGCCATCACCTCCACCCCTGCTGAGTGCTCTTCAGAGCCAC  
CCCGAGGAGGAGCCACTTCTTGTGATGGTCTACAGCCTGCTAGCCATCACCAACAACCCAG

## FIGURE 2BBBB

GAGTCAGAGTCACTGTCAGAGGAGCTGCAGAACGCTGGGCTGCTGGAGCACATCCTGGAG  
CACCTCAACAGCTCCCTCGAAAGCAGGGACGTCTGCGCCAGCGGCTGGGCTGCTCTGG  
GCCCTCCTGCTGGAGGACCCCATCTTTGGCACTCCAGCGCCCCAGGAAAAAGAGAGCTCCA  
AACCACGGAAAGCCCCGGGAAACCCAAGAACCCTGCCAGCACCCAAAGTATCATTGTGAAC  
AAGGCCCCCTTGGAGAAGGTCCCGGACCTCATCAGCCAGGTGTTGGCCACCTACCCCTGGC  
GATGGGGAAATGGCAGAAGCCAGCTGCGGAGTCTTCTGGCTGCTGTCCCTGCTGGGCTGC  
ATCAAGGAGCAGCAGTTTGAACAAGTGGTGGCGCTGCTCCTGCAAAGCATCCGGCTGTGC  
CAGGACAGAGCCCTGCTGGTGAACAATGCCTACCGGGGACTGGCCAGCCTGGTGAAGGTG  
TCAGAGCTGGCGGCCTTCAAGGTGGTGGTGCAGGAGGAGGGCGGCAGTGGCCTCAGCCTC  
ATCAAGGAGACCTACCAGCTCCACAGGGACGACCCGGAGGTGGTGGAGAACGTGGGCATG  
CTGCTGGTCCACCTGGCTTCCTATGAGGAGATCCTGCCGGAGCTGGTGTCCAGTAGTATG  
AAGGCCCTGCTCCAGGAGATCAAGGAGCGCTTCACCTCCAGCCTGGTGAAGTACAGCAGC  
GCCTTCAGCAAACCAGGCCTCCCTCCAGGTGGAAGCCCCCAGCTGGGGTGCACCACGTCT  
GGGGGACTGGAATAG

SEQ ID NO: 105\_AA118352\_M SGK071\_M

CAGAAGAAGACCCCTGCCAGAAGTCCTGGATGGCTCCTGAAGCTCTCAAATTCTCCTTCT  
CCACCAAATCCGACATCTGGTCTCTGGGCTGCATCATTCTAGACATGGCCACTTGCTCCT  
TCCTGAACGACACAGAAGCCATGCAACTGCGGAAGGCCATCCGCCATCATCCAGGCAGCC  
TGAAGCCCATCCTGAAAACCATGGAGGAGAAGCAAATCCCTGGTACAGATGTCTACTATT  
TGCTTCTGCCCTTCATGTTGCATATCAACCCCTCCGATCGACTGGCAATCAAGGATGTGA  
TGCAAGTCACCTTCATGAGCAACTCCTTCAAAGCTCCTCTGTTGCGCTGAATATGCAGC  
GGCAGAAGGTCCCCATCTTCATCACTGACGTGCTGCTTGAAGGCAACATGGCCAACATCT  
TAGGCAGCTGGCTGTGTGCTTCCTTTGTGAACGACAGCAGGCACTGTGACTCAGGGATTG  
GCTCGCAGAGACTTGGGTTTGATTTTCAGTCAGTCTCTTGGACAGAGCACCCCTCTGAAAG  
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TCAGCATCATAAAGCAGCATGGGCGGATCCTGGATATTCTGCTCAGCACCTGCTCCCTTC  
TGCTGCGTGTCTTGGCCAAGCACTGGCAAAGGACCCAGAAGCTGAGATCCCAAGGAGCA  
GTTTGATCATCTCCTTCCTGATGGATACCTTGCGGAGCCATCCTAACTCTGAAAGGCTTG  
TTAATGTGGTCTACAACGTGCTTGCCATTATTTCCAGCCAAGGACAGATCTCAGAAGAGC  
TGGAAGAGGAGGGGTTGTTTCAGCTTGCCCAAGAGAACCTGGAGCACTTCCAAGAGGACA  
GGGACATCTGCCTCTCTATCCTGAGCCTGCTCTGGTCCCTCCTGGTAGATGTTGTCACTG  
TGGACAAAGAGCCCTTGGAGCAGCTCTCTGGCATGGTCACTTGGGTGCTGGCTACTCATC  
CGGAGGACGTGGAAATAGCAGAGGCTGGCTGTGCGGTGCTCTGGCTGCTGTCTTGTGG  
GCTGCATAAAGGAGAGTCAGTTTGAGCAGGTGGTAGTGCTGCTCCTGAGAAGCATCCAGC  
TGTGCCCTGGCAGAGTACTGCTGGTGAACAATGCATTCCGTGGCTTGGCCAGCCTCGCAA  
AGGTGTCCGAACCTGGTGGCCTTCCGAATAGTAGTACTGGAAGAGGGCAGCAGCGGCCTCC  
ACCTCATCCAAGATATCTACAAGCTCTACAAGGATGACCCTGAGGTGGTGGAGAACCTCT  
GCATGCTGTTGGCCATCTGACCTCCTACAAGGAGATCCTGCCAGAGATGGAGTCTGGAG  
GCATCAAAGACCTAGTCCAGGTGATCCGGGGGCGCTTTACCTCCAGCCTGGAGCTGATTT  
CTTACGCTGATGAGATACTCCAGGTACTGGAAGCAAATGCACAACCTGGCCTCCAGGAGG  
ATCAGCTTGAGCCTCCTGCAGGGCAGGAAGCCCCACTGCAGGGAGAGCCCTCTTCAGGC  
CCTGACATGCTGCCCTTCTGGTCTGTGGTAAGAGAAAGTATCACTAGGTCCAGTATTAA  
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SEQ ID NO: 106\_018653.9\_H

GGCCGGGGTGGGGCGCGGGGCATGCGCGCGGGCTGGGCAGGGGGCGCGGGGGCGCAGA  
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GCCGGCCGGGGGAGGGGAGCGATGCGGGCGCCGGCGGGCGGCAGTGCGCGCGGGTTTCTG

## FIGURE 2CCCC

CGCCTCCTTCCTGCTGGGCTCCGTCTCAACGTGCTCTTCGCTCCGCGGTGCGAGCCTCCG  
 AGGCCAGGCCAGTCCCCCTGAGCCTTCGCCGCGCCCGGGTGCAGGCGCTGCGGGGGCCGC  
 GGGGAGCTGGCCCGGCAGATCCGGGCGCGCTACGAGGAGGTGCAGCGCTATTCCCGCGGG  
 GGCCCCGGGCGCGGGCGGGCCGGGAGCGGCGGCGCTGATGGACCTGGCTCCGGGC  
 GGGCCCGGCTGCCGCGCCCCCGGCCCTTGGGCGCGCGCTGTCCGACGGCGCCCCA  
 GGCTGGCCCCCGGCTCCCGGCCAGGCTCCCCCGGCCCGGGCCCGCGCTGGGCTGCGCC  
 GCGCTTCGCAACGTGTCCGGCGCGCAGTACATGGGCTCAGGCTACACCAAGGCCGTGTAC  
 CGGGTCCGCCTGCCCGCGGTGCCGCGGTGGCGCTCAAGGCGGTGGACTTTAGCGGCCAC  
 GATCTGGGCAGCTGCGTGCGCAGTTCGGGGTACGAGGGGCTGCTATCGGCTGGCGGCC  
 CACAAGCTGCTTAAGGAGATGGTGTCTGCTGGAGCGGCTGCGGCACCCCAACGTGCTGCAG  
 CTCTATGGCTACTGCTACCAGGACAGCGAGGACATCCCAGACACCCTGACCACCATCACG  
 GAGCTGGGCGCCCCCTGTAGAAATGATCCAGCTGCTGCAAACTTCCTGGGAGGATCGATT  
 CGAATCTGCCTGAGCCTGGGCGCGCTCCTCCACCACCTGGCCCACTCCCCACTGGGCTCC  
 GTCACCTCTGCTGGACTTCCGCCCTCGGCAGTTTGTGCTGGTGGATGGGGAGCTCAAAGTG  
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 CTCGAGTTTCCGGCCAGGAACCTTCACCCTGCCCTGCTCAGCCCAGGGCTGGTGCGAGGGC  
 ATGAACGAGAAGCGGAACCTCTATAATGCCTACAGGTTTTTCTTCACATACCTCCTGCCT  
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 GACAGCACCATCCCCCAGGAAGACTACCGCTGCTGGCCATCCTACCACCACGGGAGCTGC  
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 CGGGCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTCGGCAGCTGGTCTTTTTTCAAG  
 ACTGGATGGAGCCAAGTGGTCCCTGATCCCAACAAGACCACATATGTGAAGGCCTCTGGC  
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 GAGGGAGTGACTTGCACTGGCAGCACTGCATGTACCTGGGAACCCCTGCAGACAAAGCT  
 AACATCCCAGACAGACAGATGTGACCAGGACAAACGTGCAATAATGCCAAATGTTAAAAT  
 GTGAGTTTACCAGCCTAGCTATGGGACTGCTGGCTCCTAGTCCAGGAATCATGGGGGTAT  
 GACTGCCTCTCCAACCCTGTGGGCTGTAAGCAAGCTCAGGCTAGTCTCCCCACTGGGGGC  
 TGTGCCCTCCCTGGGACGGTTCCGTGGGCAGCCCCATCACTGTGTTCAATAGTGTGAGA  
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 AGATGCTCCAGGATGTGGGTGATTCTGTACCTGGGGAGGCTATCTCTGACCTCCCGACAG  
 GGGACACTCCCAGGCCAGCCAGGGGTGAGGGGCAGAGGTGCACACCTCAGCATGAGCCA  
 AGACTGGGGTCAGGGAGCAGGTGTGGTTTGAGCCAGGACCTGGGGCGGGGTGGGGCCGG  
 GGCCTTTCTGCCTCATTTGCTTTCAATGAAAGCCTCAAAGCAGCCAAAACCAGGCTTTCC  
 CCCTTCCTCGAGTTTGAATATCCAGAATCTTTTGTACTTCTTGTTGGTTAAATTGTTTAT  
 TTTTGTAATAAATAAATAAATTAGTTAATAAATGATGTTTCACAGCAAACCTCTCCC  
 T

SEQ ID NO: 107\_AA396601\_M

CCACGCGTCCGGGCTGCGCCGCGCTCCGCAACGTGTCTGGCGCGCAGTACGTGGGCTCAG  
 GCTACACTAAGGCTGTGTACCGGGTCCGCCTGCCCGGCGGCGCCGCGGTGGCGCTTAAAG  
 CAGTGGACTTCAGCGGCCACGATCTGGGCAGCTGCGTGCGCGAGTTCGGGGCGCGAAGGG  
 GCTGCTATCGCCTGGCGGCCACAAAGCTGCTCAAAGAGATGGTGTCTGGAGCGGCTGC  
 GGCACCCCAACGTGCTGCAGCTCTATGGCTATTGCTACCAAGACAGTGAGGGCATCCCA  
 ACACGCTGACCACCATCACAGAGCTGGGTGCCCTGTGGAGATGATCCAGCTGTTGCAGA  
 CTTCCTGGGAGGATCGATTCCGAATCTGCCTCAGCCTTGCGCGCCTCTCCACCACCTGG  
 CCCACTCCCCGCTGGGCTCGGTACCCCTGCTTGACTTCGCGCCTCGGCAGTTTGTGCTAG  
 TGAACGGGGAGCTGAAAGTGACAGACCTGGATGATGCCCGCGTGGAAGAGACACCGTGCA

## FIGURE 2DDDD

CCAGCAGTGCCGACTGCACGCTAGAGTTTCCAGCCAGGAACTTCAGCCTGCCCTGCTCGG  
CCCAGGGGCTGCTGCGAGGGCATGAATGAGAAACGGAACCTCTACAATGCCTACAGSTTCT  
TCTTCACATACCTCCTGCCACACAGTGCCCCGCTTCCCTCCGACCTCTCCTGGATAGCA  
TCGTCAATGCCACGGGAGAGCTCGCCTGGGGGGTGGATGAGACCCTGGCCCAGCTGGAGA  
CAGCGCTACACTTGTTCCGAAGTGGGCAGTACCTGCAGAACTCTACAAGCAGCAGGGCTG  
AGTACCAGCGCATCCCCGACAGTGCCATCACACAGGAGGACTATCGCTGCTGGCCATCCT  
ATCACCACGGCGGCTGCCTCCTGTCCGTGTTCAACCTGGCTGAGGCTATAGATGTCTGTG  
AGAGCCATGCTCAGTGTCTGTCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTGCGA  
AGCTGGTCTTTTTTAAGACTGGATGGAACCAAGTGGTCCCTGATGCCGGCAAGACCACAT  
ATGTGAAGGCCCTGGTTGACTGGTTGTGGGCTCAGCTGACCAGCTGGGCTTGCCTGCTG  
CAGGCGTGACTTGCATCCCACCTGGGAACCCCTGCAGACAAAAGCTAGCTCCCAGAGCAA  
CTGATGTGACCAGGACAAAACGTGCAATATGCAAAAATGTTAAAATGTGAGTTTGCCAGC  
TTCAGTCCCAGACTGGTTGGAACCCGATTGCCTCTCTGGAGCTGTAGGCTGTGAGCAGGG  
CTCAGGCTGGTCTTAAGTGGGACAGTCCCGTGGGCAGCCATTACTGCATTTCATGCTTTG  
AGAATGTAGCCAGAACACTGCTGCTGCATAAGCCACCGTGGGCAGGAGCTGCCTGGGGAC  
AACCAGTCTCAGAGTGCTCTCTCAGCTCAGCTCCGCTCCAAATGGAGAGCGCGGGATGCG  
GAGATGTGAGTGAACCAGCACTGGGAAGAAGGCTCTCGGGCCTCTCCCTAGAGGTTGCTC  
CTAGGCCAGCCCCGAGGCCGTGGGCAGCAGTGTCTGCATCCATATGAGCCAAGACTAGAG  
TGGAGGAGCAGATTGCATTGAGCCAGGACTGGGGTGGGGGTAGGGTCGGGGCCTCTCTG  
CCTCATTTGCTTTCAGTGAAAGCCAGGGAGCAGCCGCAGCCAGGCTCCTCCCCTCCTGG  
AGGCCAGGCTCCTCCCCCTCCTGGAGGCCAGGCTCCTCCCCCTCCTGGAGTTTGCGTACC  
CAGAAGCTTTTATACTTCTCGTTTCATTAAATTGTTTATTTTTGTAAAAAAAATTAAT  
CAATTAATAAAATGATGTTTTGTGAC

SEQ ID NO: 108\_VRK3\_H

ATGATCTCCTTCTGTCCAGACTGTGGCAAAAGTATCCAAGCGGCATTCAAATTCTGCCCC  
TACTGTGGAAATTCTTTGCCTGTAGAGGAGCATGTAGGGTCCCAGACCTTTGTCAATCCA  
CATGTGTATCCTTCCAAGGCTCAAAGAGAGGGCTGAACTCCAGTTTTGAAACCTCTCCT  
AAGAAAGTGAAATGGTCCAGCACCGTCACCTCTCCCCGATTATCCCTCTTCTCAGATGGT  
GACAGTTCTGAGTCTGAAGATACTCTGAGTTCCTCTGAGAGATCCAAAGGCTCCGGGAGC  
AGACCCCCCAACCCCCAAAAGCAGCCCTCAGAAGACCAGGAAGAGCCCTCAGGTGACCAGG  
GGTAGCCCTCAGAAGACCAGCTGTAGCCCTCAGAAGACCAGGCAGAGCCCTCAGACGCTG  
AAGCGGAGCCGAGTGACCACCTCACTTGAAGCTTTGCCACAGGGACAGTGCTGACAGAC  
AAGAGTGGGCGACAGTGGAAGCTGAAGTCCTTCCAGACCAGGGACAACCAGGGCATTTCTC  
TATGAAGCTGCACCCACCTCCACCCTCACCTGTGACTCAGGACCACAGAAGCAAAAGTTC  
TCACTCAAACCTGGATGCCAAGGATGGGCGCTTGTTCAATGAGCAGAACTTCTTCCAGCGG  
GCCGCCAAGCCTCTGCAAGTCAACAAGTGGGAAGAAGCTGTACTCGACCCCACTGCTGGCC  
ATCCCTACCTGCATGGGTTTCGGTGTTCACCAGGACAAATACAGGTTCTTGSTGTTACCC  
AGCCTGGGGAGGAGCCTTCAGTCGCGCCTGGATGTGAGCCCAAGCATGTGCTGTGAGAG  
AGGTCTGTGCTGCAGGTGGCCTGCCGGCTGCTGGATGCCCTGGAGTTCCTCCATGAGAAT  
GAGTATGTTTCATGGAAATGTGACAGCTGAAAATATCTTTGTGGATCCAGAGGACCAGAGT  
CAGGTGACTTTGGCAGGCTATGGCTTCGCCTTCCGCTATTGCCCAAGTGGCAAACACGTG  
GCCTACGTGGAAGGCAGCAGGAGCCCTCACGAGGGGGACCTTGAGTTTCATTAGCATGGAC  
CTGCACAAGGGATGCGGGCCCTCCCGCCGACGACCTCCAGAGCCTGGGCTACTGCATG  
CTGAAGTGGCTCTACGGGTTTCTGCCATGGACAAATTGCCTTCCCAACACTGAGGACATC  
ATGAAGCAAAAACAGAAGTTTGTGTGATAAGCCGGGGCCCTTCGTGGGACCCTGCGGTGAC  
TGGATCAGGCCCTCAGAGACCCTGCAGAAGTACCTGAAGGTGGTGTGAGCCCTCAGGTAT  
GAGGAGAAGCCGCCCTACGCCATGCTGAGGAACAACCTAGAAGCTTTGCTGCAGGATCTG  
CGTGTGTCTCCATATGACCCCATTEGGCTCCCGATGGTGCCCTAG

## FIGURE 2EEEE

SEQ ID NO: 109\_S71575\_M VRK3\_M

CCATCCCCACCTGTATCGGCTTTGGCATTACACCAGGACAAGTACAGGTTCTAGTATTCC  
CCAGCCTGGGGAGGAGCCTTCAGTCAGCCCTGGATGACAACCCAAAGCATGTGGTATCAG  
AGAGATGTGTGCTTCAGGTGGCCTGCAGGCTGCTGGATGCTCTGGAGTATCTCCATGAAA  
ATGAGTATGTTACGGGAACCTGACAGCTGAGAATGTCTTTGTGAATCCAGAGGATCTGA  
GCCAGGTGACCCTGGTGGGCTATGGCTTCACCTACCGATACTGCCAGGTGGCAAACACG  
TGGCCTACAAAGAAGGCAGCAGGAGTCCACACGATGGGGACTTGGAGTTCATTAGCATGG  
ACCTGCACAAGGGATGCGGACCCTCCCGCCGACGCGATCTCCAGACCTTGGGCTACTGTA  
TGCTCAAGTGGCTTTATGGGTCCCTGCCATGGACAAATTGCCTTCCCAACACCGAAAAGA  
TAACTAGGCAGAAGCAGAAGTATCTGGACAGCCCCGAGCGCCTCGTGGGACTGTGTGGCC  
GCTGGAACAAGGCCTCAGAGACCCTGCGGGAGTACCTGAAGGTGGTGTATGGCCCTCAATT  
ATGAGGAGAAGCCACCCTATGCCACGCTGAGGAACAGCCTAGAAGCTCTGCTGCAGGATA  
TGCGGGTGTACCCCTATGACCCTCTGGACCTCCAGATGGTGCCTTAGATGGAATCCAGAG  
CTTCCGACTTGCAGCTTGAAGTAGAACATGAAGTAGTGTGACTGGAGGCCTGTTTGAAC  
CATAGCTCCTAAAAGAATCCCTTGAATGTGCATTCTCACCCTCCCTTAGGACATATGAA  
TCAGCACTTGTGTTGGGGAACCTGAGTCATGTGTAATGTGAACTCCTCCCTGTCTC  
AGCTCTGGCAGCTGTGGATGGAGGTAAGTGGATGCTGGCGGCGGCGGCGGCGGAGCAGCCAC  
TCCACTCCCTATGGCATTCTGTGATGGCATAATAAACTGTTTTTAATC

SEQ ID NO: 110\_AA45427\_H

ATGGGCCACGCGCTGTGTGTCTGCTCTCGGGGAAGTGTGATCATTGACAATAAGCGCTAC  
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CATGATGGACACTTCTACGCCCTGAAGCGAATCCTGTGTACGAGCAGCAGGACCGGGAG  
GAGGCCCAGCGAGAAGCCGACATGCATCGCCTCTTCAATCACCCCAACATCCTTCGCCTC  
GTGGCTTACTGTCTGAGGGAACGGGGTGCTAAGCATGAGGCCTGGCTGCTGCTACCATTC  
TTCAAGAGAGGTACGCTGTGGAATGAGATAGAAAGGCTGAAGGACAAAGGCAACTTCCTG  
ACCGAGGATCAAATCCTTTGGCTGCTGCTGGGGATCTGCAGAGGCCTTGAGGCCATTTCAT  
GCCAAGGGTTATGCCACAGAGACTTGAAGCCCACCAATATATTGCTTGGAGATGAGGGG  
CAGCCAGTTTTAATGGACTTGGGTTCCATGAATCAAGCATGCATCCATGTGGAGGGCTCC  
CGCCAGGCTCTGACCCTGCAGGACTGGGCAGCCAGCGGTGCACCATCTCCTACCGAGCC  
CCAGAGCTCTTCTGTGTCAGAGTCACTGTGTGTCATCGATGAGCGGACTGATGTCTGGTCC  
CTAGGCTGCGTGCTATATGCCATGATGTTTGGGGAAGGCCCTTATGACATGGTGTTCCAA  
AAGGGTGACAGTGTGGCCCTTGCTGTGTCAGAACCAACTCAGCATCCCACAAAGCCCCAGG  
CATTCTTCAGCATTGCGGCAGCTCCTGAACTCGATGATGACCGTGGACCCGCATCAGCGT  
CCTCACATTCTCTCCTCCTCAGTCAGCTGGAGGCGCTGCAGCCCCAGCTCCTGGCCAA  
CATACTACCCAAATCTGA

SEQ ID NO: 111\_H05721\_H

CCCTGAGGCACCGCCCCAAGTTTGGTGTGACCGGCGGGGACGCGCGGTGGTGGCGGCAGC  
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CGGCCTGCAGCTGGGTGAGCGCTGCTGCTGCGCTTCACGGGCAAGCCCGGCGGGGCTA  
CGGCTTGGGGGGGGGGGGCGGGCGGGGCTGTGTCCGCGGGGAGCGTCCAGGCTGGGG  
CGCAGGAACGGGGCGGAGCCTCGCAGGGTGGGGCTCGGGCTCCCTAACCGTCTCCGCTT  
CTTCCGCCAGTCGGTGGCCGGGCTGGCGGCGCGGTTGCAGCGGCAGTTCTGTGGTGGGGG  
CTGGGGCTGCGCGGGGCCCTTGCGGGCGGGCAGTCTTTCTGGCCTTCGGGCTAGGGCTGGG  
CCTCATCGAGGAAAAACAGGCGGAGAGCCGGCGGGCGGTCTCGGCCTGTGAGGAGATCCA  
GGCAATTTTTTACCCAGAAAAGCAAGCCGGGGGCTGACCCGTTGGACACGAGACGCTTGCA  
GGGCTTTCCGCTGGAGGAGTATCTGATAGGGCAGTCCATTGGTAAGGGCTGCAGTGCTGC  
TGTGTATGAAGCCACCATGCCTACATTGCCCCAGAACCTGGAGGTGACAAAGAGCACCGG  
GTTGCTTCCAGGGAGAGGCCAGGTACCAAGTGCACCAGGAGAAGGGGAGGAGCGAGCTCC

## FIGURE 2FFFF

GGGGGCCCCCTGCCTTCCCCCTTGGCCATCAAGATGATGTGGAACATCTCGGCAGGTTCCCTC  
CAGCGAAGCCATCTTGAACACAATGAGCCAGGAGCTGGTCCCAGCGAGCCGAGTGGCCCTT  
GGCTGGGGAGTATGGAGCAGTCACTTACAGAAAAATCCAAGAGAGGTCCCAAGCAACTAGC  
CCCTCACCCCAACATCATCCGGGTCTCTCCGCGCCTTCACTCTTCCGTGCCGCTGCTGCC  
AGGGGCCCTGCTCGACTACCCCTGATGTGCTGCCCTCACGCCTCCACCCCTGAAGGCCTGGG  
CCATGGCCGGACGCTGTTCCCTCGTTATGAAGAACTATCCCTGTACCCCTGCGCCAGTACCT  
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CGTGGACCATCTGTTTCAACAGGGCATCGCGCACAGAGACCTGAAATCCGACAAACATCCT  
TGTGGAGCTGGACCCAGACGGCTGCCCTGGCTGGTGTATCGCAGATTTTGGCTGCTGCCT  
GGCTGATGAGAGCATCGGCCTGCAGTTGCCCTTACGACAGCTGGTACGTGGATCGGGGCGG  
AAACGGCTGTCTGATGGCCCCAGAGGTGTCCACGGCCCCGTCTGGCCCCAGGGCAGTGAT  
TGACTACAGCAAGGCTGATGCCTGGGCAGTGGGAGCCATCGCCTATGAAATCTTCCGGGCT  
TGTCAATCCCTTCTACGGCCAGGGCAAGGCCACCTTGAAAGCCGCAGCTACCAAGAGGC  
TCAGCTACCTGCACTGCCCCGAGTCAGTGCCTCCAGACGTGAGACAGTTGGTGAGGGCACT  
GCTCCAGCGAGAGGCCAGCAAGAGACCATCTGCCCGAGTAGCCGCAAATGTGCTTCATCT  
AAGCCTCTGGGGTGAACATATTCTAGCCCTGAAGAATCTGAAGTTAGACAAGATGGTTGG  
CTGGCTCCTCCAAACATCGGCCGCCACTTTGTTGGCCAACAGGCTCACAGAGAAGTGTTG  
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GAATTACTAAAAGAACATGGCATCCTCTGTGTCTGTGATGGTCTGTGAATGGTGAGGGTGG  
GAGTCAGGAGACAAGACAGCGCAGAGAGGGCTGGTTAGCCGGAAAAGGCCTCGGGCTTGG  
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AGTGAATGGCCAAGCTGGTCTAGTAGATGAGGCTGGACTGAGGAGGGGTAGGCCTGCATC  
CACAGAGAGGATCCAGGCCAAGGCACCTGGCTGTCACTGGCAGAGTTTGGCTGTGACCTTT  
GCCCCTAACACGAGGAACCTCGTTTGAAGGGGGCAGCGTAGCATGTCTGATTTGCCACCTG  
GATGAAGGCAGACATCAACATGGGTGAGCACGTTCACTTACGGGAGTGGGAAATTACATG  
AGGCCTGGGCCTCTGCGTTCCCAAGCTGTGCGTTCTGGACCAGCTACTGAATTATTAATC  
TCACTTAGCGAAAGTGACGGATGAGCAGTAAGTAAGTAAGTGTGGGGATTTAACTTGAG  
GGTTTCCCTCCTGACTAGCCTCTCTTACAGGAATTGTGAAATATTAATGCAAATTTACA  
ACTGCAGATGACGTATGTGCCTTGAAGTGAATATTTGGCTTTAAGAATGATTCTTCTTAT  
ACTCTGAAGGTGAGAATATTTTGTGGGCAGGTATCAACATTGGGGAAGAGATTTTCATGTC  
TAACTAATACTTTATACATGATTTTTAGGAAGCTATTGCCTAAATCAGCGTCAACATG  
CAGTAAAGGTTGTCTTCAACTGACAAAA

SEQ ID NO: 112\_AI086865\_H

AATGAGATGGAGAAGTACGAGCGGATCCGAGTGGTGGGGAGAGGTGCCTTCGGGATTGTG  
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AACCACCCCAATGTCATTGAGTACTACGAGAACTTCCCTGGAAGACAAAGCCCTTATGATC  
GCCATGGAATATGCACCAGGCGGCACTCTGGCTGAGTTTATCCAAAAGCGCTGTAATTCC  
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GTGCACACCCACCTCATCCTGCACCGAGACCTCAAGACCCAGAACATCCTGCTTGACAAA  
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CGGTACAGCCCTGAGCTTCCGCCAGCTGGTCTGAGTCTACTCAGCCTGGAGCCTGCCAG  
CGGCCACCACTCAGCCACATCATGGCACAGCCCCCTCTGCATCCGTGCCCTCCTCAACCTC  
CACACCGACGGCAGAGAAGTCCGTGGCCCCCAGCAACACAGGGAGCAGGACCAACAGTGT  
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GGTGTGGCGTCCAGCACTGATGTGTCTACCTTCTCTGAAGGTGACTGCAAGGAGCCTGAC  
AAGTGCTGCTGGAGACACAAGCAGTGCCTGGGCACATCATCTACCCCTTTCGCTCTGAC  
TGTGTCCGCCACAGCCTGCACCTACACTCTGTCAACCACTGCAACTGTAATTCTAGGCTG  
AAGGACTCTTCAGAGGATAGCAGCAGCTCCCGGGGCGCGGGCCCAACCTGCTCCCATGTCT  
ATCGAGTCCCTTTGCTTTGAGCTCACACCGGAGGAGGAGCATGTGGAGCGATTCCGGTAT  
GGCTGGTGCAAAAGCTACAGACCTGTCTCTGTGGCAGTGATCCACCATCCACTCTACCAT  
GAGTGTGGGGCAGATGATCTAAATGXAAAGAAGAGGAAGAGGAGGAGGAGGAAAAGCAAG  
CCCCCATCCCGACACAGGTGGGGCCCCGCCACCGCCTCCCCTGACCTAGGCACCAGCATG  
GCCACTGGTACCCCTGACTCCACAGCGCCCATCACCATCTGGCGCTCTGAGAGCCCCACA  
GGGAAGGGTCAGGGCAGCAAGGTGATCAAGAAGGTAAAGAAGAAAAAGGAAAAAGAGAAA  
GACAAGGAGGAGATGGATGAGAAGGCCAAAGCTGAAGAAAAAAGCCAAGAAAGGCCAGTTG  
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AGCGCAAGACAGCTGGCCAGGATGTCCGAGTCCAGCCCAGAAAGCCGGGAAGAGCTGGAG  
AGCGAGGACAGTTACAATGGCCGGGGGCAGGGAGAAGTGTCCAGCGAGGATATTGTGGAA  
TCATCATCGCCCAGGAAGAGAGAGAACACAGTCCAGGCCAAAAAGACAGGGGGCAAAGCCC  
TCACAAGCCAGGAAGGTAAACAAGAGAAAAATCTCCCCCAGGATCAAACCCCAACCTCAGT  
TGAGGCCAGGGTGGTCAGGGTGCAGAATAAATGCCATCGAGCCTGTGGCTGGCCCTCTGC  
TGCTGTTCTCTCCCTCCAACCTGGCTGTTTCTTGCGGGGCAAGGGGTGGGCTCAGGGCTG  
CAGGGGTTTCTCAAAGGCAATCCAGCTTTCACAAAGGAAGCCCATGGGAAGGCAGGTGGG  
AGGGAAAGGAAGGGGCACAGCCCTATTTCTTCCCTACCTGCTAGGACAAGGTGGAAGAGTG  
TATCTGGGGTGGGAAGGAGGGCTTCCCCTCTCTGCTGCGAGAGACTGGTCTGTGTGAAAT  
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CCC

ATGTCGGGTGCTGGGCGAGTACGAGCGACACTGCGATTCCATCAACTCGGACTTTGGGAGC  
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GGCGGCGGCGCGGCGGAGCAGGAGGAACTGCACTACATCCCCATCCGCGTCCTGGGGCCGC  
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AAGGAAGTCGATTTGACCCGGCTGTCTGAGAAGGAACGTCGTGATGCCTTGAATGAGATA  
GTTATTCTGGCACTGCTGCAGCACGACAACATTATTGCCCTACTACAATCACTTTCATGGAC  
AATACCACGCTGCTGATTGAGCTGGAATATTGTAATGGAGGGAACTGTATGACAAAATC  
CTTCGTGAGAAGGACAAGTTGTTTGAGGAAGAGATGGTGGTGTGGTACCTATTTTCAGATT  
GTTTCAGCAGTGAGCTGCATCCATAAAGCTGGAATCCTTCATAGAGATATAAAGACATTA  
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CCCATTGCTGTAGTAACATCACGAACCACTGAAGTCTATGTTTGGGGTGGTGGAAAATCC  
ACCCCCCAGAACTGGATGTTATCAAGAGTGGCTGTAGTGCCCCGGCAGGTCTGTGCAGGG  
AATACCCACTTTGCTGTGGTCAAGTGGAGAAGGAACTGTACACTTGGGTGAACATGCAA  
GGAGGCACTAACTCCATGGTCAGCTGGGCCATGGAGACAAAGCCTCCTATCGACAGCCA  
AAGCATGTGGAAAAGTTGCAAGGCAAAGCTATCCGTCAGGTGTATGTGGTGTATGATTTT

## FIGURE 2HHHH

ACTGTCTGTGTGACTGATGAGGGTCAGCTCTATGCCTTCGGATCAGATTATTATGGCTGC  
ATGGGGGTGGACAAAGTTGCTGGCCCTGAAGTGCTAGAACCCATGCAGCTGAACTTCTTC  
CTCAGCAATCCAGTGGAGCAGGTCTCCTGTGGAGATAATCATGTGGTGGTTCTGACACGA  
AACAAAGGAAGTCTATTCTTGGGGCTGTGGCGAATATGGACGACTGGGTTTGGATTTCAGAA  
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CAATGTGGCTGTGATGGGACATTTCTGTTGACCCAGTCAGGCAAAGTGCTGGCCTGTGGA  
CTCAATGAATTCAATAAGCTGGGTCTGAATCAGTGCATGTCGGGAATTATCAACCATGAA  
GCATACCATGAAGTTCCCTACACAACGTCTTTACCTTGGCCAAACAGTTGTCCTTTTAT  
AAGATCCGTACCATTTGCCCCAGGCAAGACTCACACAGCTGCTATTGATGAGCGAGGCCGG  
CTGCTGACCTTTGGCTGCAACAAGTGTGGGCAGCTGGGCGTTGGGAACTACAAGAAGCGT  
CTGGGAATCAACCTGTTGGGGGGACCCCTTGGTGGGAAGCAAGTGATCAGGGTCTCCTGC  
GGTGATGAGTTTACCATTGCTGCCACTGATGAGAAAGTATTGAATTCTAAGACCATCCGT  
TCCAATAGCAGTGGCTTATCCATTGGAAGTGTGTTTCAGAGCTCTAGCCCGGGAGGAGGC  
GGCGGGGGCGGCGGTGGTGAAGAAGAGGACAGTCAGCAGGAATCTGAAACTCCTGACCCA  
AGTGGAGGCTTCCGAGGAACAATGGAAGCAGACCGAGGAATGGAAGGTTTAAATCAGTCCC  
ACAGAGGCCATGGGGAACAGTAATGGGGCCAGCAGCTCCTGTCTGGCTGGCTTCGAAAG  
GAGCTGGAAAATGCAGAATTTATCCCCATGCCTGACAGCCCATCTCCTCTCAGTGCAGCG  
TTTTCAGAATCTGAGAAAGATACCCTGCCCTATGAAGAGCTGCAAGGACTCAAAGTGGCC  
TCTGAAGCTCCTTTGGAACACAAACCCCAAGTAGAAGCCTCGGTAAGTGAAGTGGCC  
TTTGAATCACAACTAGTCACCTCGGCTGAATCCTGCAGTAACCTGTGCTGGGAAGGGAAC  
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TACTGGGATGTGGGTTTCTACCTGGGAGCCAGATCCTCGCCAATGACCCACCCAGGTG  
GTGCTGGCTGCAGAGCAGCTGTATAAGCTCAATGCCCCCATATGGTACCTGGTGTCCGTG  
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GCCTGTGCCAGGGCGACCAAGTGCTTGGTGCTGGTCTGGAGATGAACAAGGTGCTGCTG  
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TGGGGACCCCTGAAGGACAACGAGAGCACCATCAGTTTCTACACCCGCCAGATCCTG  
GGACTTGGCTACTTGCACGACAACCAATCGTGCACAGGGACATAAAAGGGGACAATGTG  
CTGATCAACACCTTCAGTGGGCTGCTCAAGATTTCTGACTTCGGCACCTCCAAGCGGCTG  
GCAGGCATCACACCTTGCACTGAGACCTTCACAGGAAGTCTGCAGTATATGGCCCCAGAA



## FIGURE 2III

ATCATTGACCAGGGCCACGCGGGTATGGGAAAGCAGCTGACATCTGGTCACTGGGCTGC  
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 GCCATGTTTCAGGTGGGTATGTACAAGGTCCATCCGCCAATGCCAGCTCTCTGTCGGCC  
 GAGGCCCAAGCCTTCTCCTCCGAACCTTTGAGCCAGACCCCGCCTCCGAGCCAGCGCC  
 CAGACACTGCTGGGGGACCCCTTCTGCAGCCTGGGAAAAGGAGCCGCAGCCCCAGCTCC  
 CCACGACATGCTCCACGGCCCTCAGATGCCCCCTTCTGCCAGTCCCACTCCTTCAGCCAAC  
 TCAACCACCCAGTCTCAGACATTCCCGTGCCCTCAGGCACCCTCTCAGCACCCACCCAGC  
 CCCCCGAAGCGCTGCCTCAGTTATGGGGGCACCAGCCAGCTCCGGGTGCCGAGGAGCCT  
 GCGGCCGAGGAGCCTGCGTCTCCGGAGGAGAGTTGCGGGCTGAGCCTGCTGCACCAGGAG  
 AGCAAGCGTCGGGCCATGCTGGCCGAGTATTGGAGCAGGAGCTGCCAGCGCTGGCGGAG  
 AATCTGCACCAGGAGCAGAAGCAAGAGCAGGGGGGCCGTCTGGGCAGAAACCATGTGGAA  
 GAGCTGCTGCGCTGCCTCGGGGCACACATCCACACTCCCAACCGCCGGCAGCTCGCCAG  
 GAGCTGCGGGCGCTGCAAGGACGGCTGAGGGCCAGGGCCTTGGGCCTGCGCTTCTGCAC  
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 GTGCTAGGACCGGAGGTGGAGAAGGAGGCGGTCTCACCGAGGTCAGAGGAGCTGAGTAAT  
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 GGCCCCGCTCCTCTGATGGTGACGCTGAGCCTCTTGAGGGCAGAGACTGATCGGCTGCGC  
 GAAATCCTGGCGGGGAAGGAACGGGAGTACCAGGCCCTGGTGACGCGGGCTCTACAGCGG  
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 GACCAGGGCCTGGTGAGTGGCTACAGGAACTGAATGTGGATTGAGGCACCATCCAAATG  
 CTGTTGAACCATAGCTTCAACCTCCACACTCTGCTCACCTATGCCACTCGAGATGACCTC  
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 CGAGCAGGATCCACACCAGTCACCTCTGGACCCTGA

SEQ ID NO: 115\_PAK6\_H

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 GGGACCAGCGGGTGCTCCAAGGAGAGCCTGGCGTACAGTGAAAGTGAATGGGGACCCAGC  
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 CTGAGCTCCCTCAGCCTCTCATCCAGCACCTACCCGCCGCCAGCTGGGGCTCCTCCTCC  
 GACCAGCAGCCCTCCAGGGTGTCCCATGAACAGTTTCGGGCGGGCCCTGCAGCTGGTGCTC  
 AGCCCAGGAGACCCAGGGAATACTTGCCCAACTTTATCAAAATCGGGGAAGGCTCAACC  
 GGCATCGTATGCATCGCCACCGAGAAACACACAGGGAAACAAGTTGCAGTGAAGAAAATG

## FIGURE 2JJJJ

GACCTCCGGAAGCAACAGAGACGAGAACTGCTTTTCAATGAGGTGCTGATCATGCGGGAT  
TACCACCATGACAATGTGGTTGACATGTACAGCAGCTACCTTGTGGCGATGAGCTCTGG  
GTGGTCATGGAGTTTCTAGAAGGTGGTGCCTTGACAGACATTGTGACTCACACCAGAATG  
AATGAAGAACAGATAGCTACTGTCTGCCTGTCAGTTCTGAGAGCTCTCTCCTACCTTCAT  
AACCAAGGAGTGATTACAGGGACATAAAAAGTGACTCCATCCTCCTGACAAGCGATGGC  
CGGATAAAGTTGTCTGATTTTGGTTTCTGTGCTCAAGTTTCCAAAGAGGTGCCGAAGAGG  
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GGGACAGAGGTGGACATCTGGTCCCTCGGGATCATGGTGATAGAAATGATTGATGGCGAG  
CCCCCTACTTCAATGAGCCTCCCTCCAGGCGATGCGGAGGATCCGGGACAGTTTACCT  
CCAAGAGTGAAGGACCTACACAAGGTTTCTTCAGTGCTCCGGGGATTCTAGACTTGATG  
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CTGGAATGCAGTCTCAGTGACAAGTTGTGTGTATCCAGGAGAAGCAGTATGAAGTGATT  
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CATCAATACCTGGGGAAACACAAAACCTGGTGCAGCTGGAAGGCTGCTGCACTGAAAAG  
CTGCCACTCTATATGGTGTGGAGGATGTGGCCCAGGGGGACCTGCTCGGCTTTCTCTGG  
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CCTGAAGTCCCTCCTACCAGCATCCTAGAGCATCTCCAAAGAAGGAAAATCATGAAGAGA  
CCCAGTAGCTGCACACATACCATGTACAGTATCATGAAGTCCTGCTGGCGCTGGCGTGAG  
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AGTTCTTCAGTCCTGAGCCCTACATGTGGGGCTGGAGGAGAAGTATAACGGAAAAACCTC  
TGAGTTTCACTTAGGTATAGATAAAAGAAAGATGGTCCCCCTTTTATCTGATTCTGAGAC  
AGGTAAATTCTGTTTGTACTACGTTTAATTAGAAGGTGGAGGAGTCATTTTCATGATTAA

## FIGURE 2KKKK

GAACATTCAACATGTATTGTTTCATTAAGCTAGCTTCCTAGTTCGGATTAGACTAAGGAGA  
CTAAGCCTAGAGAGTCAATGTTAGAACAGTGAAAAGAATTCTGTGTGTGTGTGTGTGTGT  
GTGTGTGTGTGCACAATAAATAGGAAATGTAGAAACCAAGCAAGAAGGCTTAGTAGCTCA  
GTCTTTAACAAGGGCTAGAAAAGAATGTAATCTGATATGGAAGGATAGCAGCTTCTAATT  
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SEQ ID NO: 117\_AA098024\_M

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CAGAGAAAGAAAATCATGAAGAGACCCAGCAGCTGCTCACATGCCATGTACAACATCATG  
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GAAGAGGGCAGAGCCGTGCATGGGGCTGCTCCCCAGGACCTGAGCAGGAACCTGGAGTTT  
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TCCCTCAACATCATTTACAGGGATCTGAAACCAGAGAACATTCTCTTGGACTGCCAGGGA  
CACGTGGTGTGACGGATTTTGGCCTCTGCAAGGAAGGTGTAGAGCCTGAAGACACCACA

## FIGURE 2LLLL

TCCACATTCTGTGGTACCCCTGAGTACTTGGCACCTGAAGTGCTTCGGAAAGAGCCTTAT  
GATCGAGCAGTGGACTGGTGGTGCTTGGGGGCAGTCCTCTACGAGATGCTCCATGGCCTG  
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TTCAGCCCCATAAACTGGGATGACCTGTACCACAAGAGGCTAACTCCACCCTTCAACCCA  
AATGTGACAGGACCTGCTGACTTGAAGCATTTTGACCCAGAGTTCACCCAGGAAGCTGTG  
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SEQ ID NO: 120\_CCRK\_H

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SEQ ID NO: 121\_TESK2\_H

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## FIGURE 2MMMM

CCCACCGCCTCCGCAGGCTAAGGAGCCGCTGCCACCAACGAGCTGTGAGGGTTACTATGC  
TCCCTCTTTGCCGCGCTCTCCTCCTCTTGCCCGCGCAGGCACCCCTCTGGCTGCTCAGTC  
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